

TCACGTAAAA AGGTATCTA GAATTATGAT GATTACTCTG CGCAAACTTC CTCTGGCGGT TGCCGTGCGA GCGGGCGGTAA TGTCTGCTCA GGCCATGGCC
AGTGCATTTT TCCCATAGAT CTTAATACTA CTAATGAGAC GCGTTTGAAG GAGACCGCCA ACGGCAGCGT CGCCCGCATT ACAGACGAGT CCGGTACCGG
MetMe tileThrLeu ArgLysLeuP roLeuAlaVa lAlaValAla AlaGlyValM etSerAlaGl nAlaMetAla
^Start of lamB signal sequence

GGTCCCGAAA CTCTGTGGG TGCTGAACTG GTTGACGCTC TGCAGTTCGT ATGTGGTGAT CGAGGCTTCC TGTTCACAA ACCGACTGGG GCTGGATCCT
CCAGGGCTTT GAGACACGCC ACGACTTGAC CAACTGGGAG ACGTCAAGCA TACACCACTA GCTCCGAAGG ACAAGTTGTT TGGCTGACCC CGACCTAGGA
GlyProGluT hrLeuCysGl yAlaGluLeu ValAspAlaL euGlnPheVa lCysGlyAsp ArgGlyPheL euPheAsnLy sProThrGly AlaGlySerSer
^Start of IGF-I (Y24L, Y31A)

CCTCTCGTCG TGCTCCCCAG ACTGGTATTG TTGACGAATG CTGCTTTCGT TCTTGGGACC TGCGTCGTCT GGAAATGTAT TGGCTCCCC TGAACCCCGC
GGAGAGCAGC ACGAGGGGTC TGACCATAAC AACTGCTTAC GACGAAAGCA AGAAGCTGG ACGCAGCAGA CCTTTACATA ACGCGAGGGG ACTTTGGGCG
SerArgAr gAlaProGln ThrGlyIleV alAspGluCy sCysPheArg SerCysAspL euArgArgLe uGluMetTyr CysAlaProL eulysProAla

TAAATCTGCT TAGAAGCTCC TAACGCTCGG TTGCCGCCCGG GCGTTTTTTTA TTGTTAACTC ATGTTTGACA GCTTATCATC GATAAGCTTT AATGCGGTAG
ATTTAGACGA ATCTTCGAGG ATTGCGAGCC AACGGCGGCC CGCAAAAAAT AACAAATTGAG TACAAACTGT CGAATAGTAG CTATTGAAA TTACGCCCATC
LysSerAla Am*

Nucleotide and Amino Acid Sequence of the lamB Signal Sequence and IGF-I (Y24L, Y31A)

FIG. 1

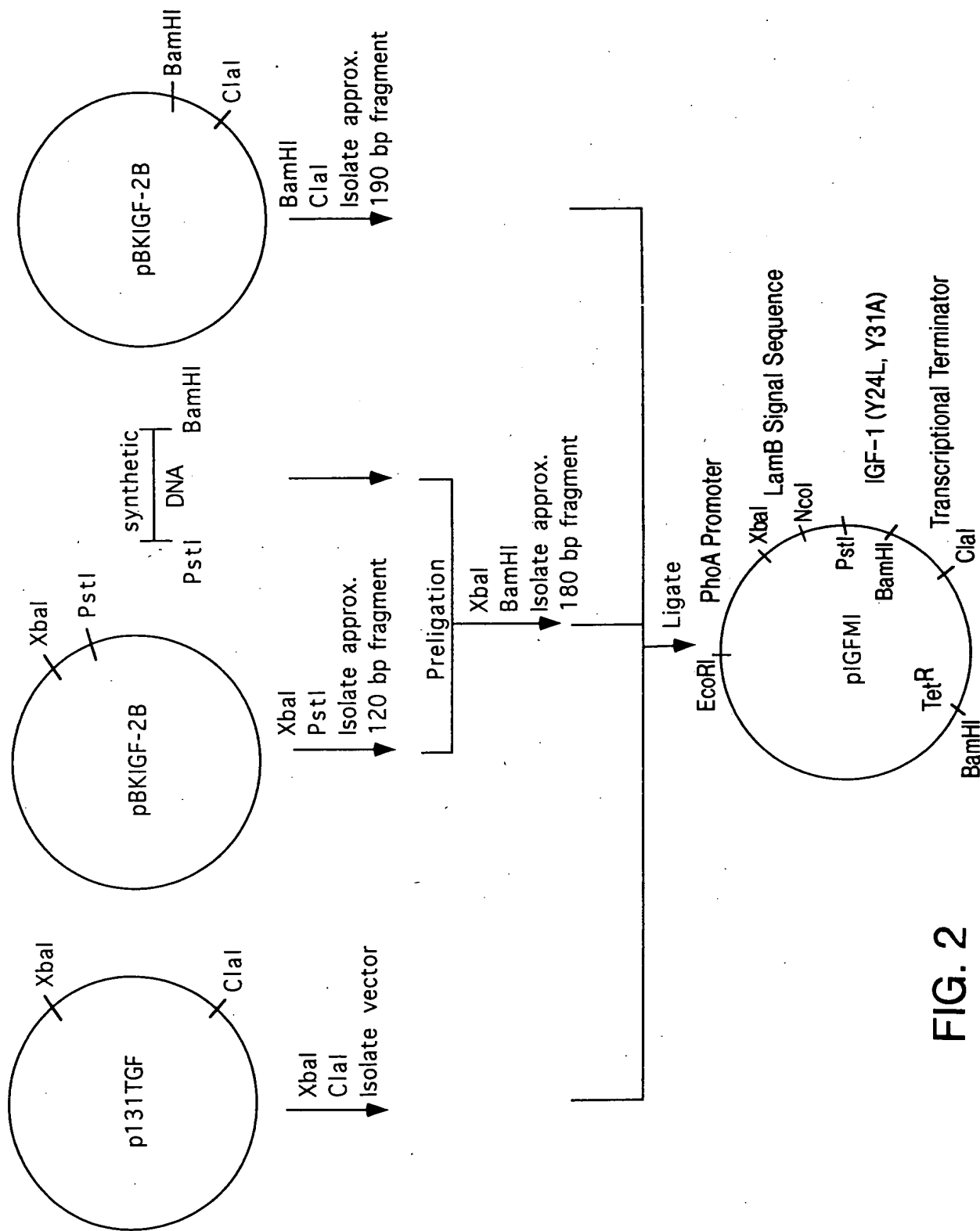


FIG. 2



plasmid IGfMI

length: 5115 (circular)

```
1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGTCTG TACTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACACGG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GAGGTTACGA AGCGTTATAC CCGGTTTTAC TGGTTGTCGC CAACTAACTA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCACTA
CCCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTTCAACA GCTGTCAATA AGTTGTCACG GCCGAGACTT ATAGTCGCTT TGTGTTTATT TTTTAATGTA TTGTAACATA GTACGCAAGT
TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CCGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATGCCGTCA

401 TCACGTAAAA AGGTATCTA GAATTATGAT GATTACTCTG CGCAAACTTC CTCTGGCGGT TGCCGTCGCA GCGGGCGTAA TGCTGCTCA GGCCATGGCC
AGTGCAATTT TCCCATAGAT CTTAATACTA CTAATGAGAC GCGTTTGAAG GAGACCGCA ACAGCGAGT ACAGACGAGT CCGGTACCGG

1 MetMe tilethrLeu ArgLysLeup roLeuAlaValAla AlaGlyValM etSerAlaGl nAlaMetAla

501 GGTCGCGAAA CTCTGTGCGG TGCTGAACCTG GTTGACGCTC TGCAAGTTCGT ATGTGCTGAT CGAGGCTTCC TGTTCAACAA ACCGACTGGG GCTGGATCCT
CCAGGGCTTT GAGACACGCC ACGACTTGAC CACTGCGGAG ACGTCAAGCA TACACCACCTA GCTCCGAAGG ACAAGTTGTT TGGCTGACCC CGACCTAGGA

26 GlyProGluT hrLeuCysG1 yAlaGluLeu ValaspAlaL euGlnPheVa lCysGlyAsp ArgGlyPheL eupHeAsnLy sProThrGly AlaGlySerSer

601 CCTCTCGTCG TGCTCCCCAG ACTGGTATTG TTGACGAATG CTGCTTTCGT TCTTGCAGCC TGCGTCGTCT GGAAATGTAT TCGGCTCCCC TGAACCCCGC
GGAGAGCAGC ACGAGGGGTC TGACCATAAC AACTGCTTAC GACGAAAGCA AGAACGCTGG ACGCAGCAGA CTTTACATA ACGCGAGGGG ACTTTGGGCG

60 SerArgAr gAlaProGln ThrGlyIlev alAspGluCy sCysPheArg SerCysAspL euArgArgLe uGluMetTyr CysAlaProL euLysProAla

701 TAAATCTGCT TAGAAGCTCC TAACGCTCGG TTGCCGCGCG GCGTTTTTTA TTGTTAACTC ATGTTTGACA GCTTATCATC GATAAGCTTT AATGCGGTAG
ATTTAGACGA ATCTTCGAGG ATTGCGAGCC AACGGCGGCC CGCAAAAAT AACAAATTGAG TACAAACTGT CGAATAGTAG CTATTGAAA TTACGCCATC

93 LysSerAla Am*

801 TTTATCAcAG TTAAATTGCT AACCGAGTCA GGCACCGTGT ATGAAATCTA ACAATGCGCT CATCGTCATC CTCGGCACCG TCACCCCTGA TGCTGTAGGC
AAATAGTGTC AATTTAACGA TTGCGTCAGT CCGTGGCACA TACTTTAGAT TGTTACCGGA GTAGCAGTAG GAGCCGTGGC AGTGGACCT ACGACATCCG

901 ATAGGCTTGG TTATGCCGGT ACTGCCGGG CTCTTGCGGG ATATCGTCCA TTCCGACAGC ATCGCCAGTC ACTATGGCGT GCTGCTAGCG CTATATGCGT
TATCCGAACC AATACGGCCA TGACGGCCCG GAGAACGCC TATAGCAGGT AAGGCTGTCG TAGCGGTGAG TGATACCGCA CGACGATCGC GATATACGCA

1001 TGATGCAATT TCTATGCGCA CCGGTTCTCG GAGCACTGTC CGACCGCTTT GGCGCGCGCC CAGTCTGCT CCGTTCCGTA CTTGGAGCCA CTATCGACTA
ACTACGTTAA AGATACGCGT GGCAAGAGC CTCGTGACAG GGTGGCGG GGTGGCGG GTCAGGACGA GCGAAGCGAT GAACCTCGGT GATAGCTGAT
```

FIG. 3A



1101 CGCGATCATG GCGACCACAC CCGTCCTGTG GATCCTCTAC GCCGGACGCA TCGTGCCCGG CATCACCCGG GCCACAGGTG CGGTTGCTGG CGCCTATATC
GCGTAGTAC CGCTGGTGTG GGCAGGACAC CTAGGAGATG CCGCCTGCGT AGCACCGGCC GTAGTGCCG CCGTGTCCAC GCCAACGACC GCGGATATAG

1201 GCCGACATCA CCGATGGGA AGATCGGGCT CGCCACTTCG GGCATCATGAG CGCTTGTTTC GCGTGGGTA TGGTGGCAGG CCCCCTGGCC GGGGACTGT
CGCGTGTAGT GGTACCCCT TCTAGCCCCG GCGGTGAAGC CCGAGTACTC CCGACCAAG CCGCACCCAT ACCACCGTCC GGGGCACCGG CCCCCTGACA

1301 TGGGCGCCAT CTCCTTGAT GCACCATTC CCGGCGCGG TTGCGCGCGG AAGCGCGCG CACCGAGTGG ATGATGACCC GACGAAGGAT TACGTCTCA CCGTATTTCC
ACCCCGGTA GAGGAACGTA CCGGTGAAG CCGCGCGCG AAGCGCGCG CACCGAGTGG CCGGAGTGG CCGACCAAG CCGCACCCAT ACCACCGTCC GGGGACTGT

1401 AGAGCGTGA CCGATGCCCT TGAGAGCCTT CAACCCAGTC AGCTCCTTC AGCTGCTGAG GGCATGACT ATCGTCGCC CACTTATGAC TGTCTTCTT
TCTCGCAGCT GGTACGGGA ACTCTCGGA GTTGGGTG TCGAGGAAG CCACCCGCG CCGTACTGA TAGCAGCGG GTGAATACTG ACAGAAGAAA

1501 ATCATGCAAC TCGTAGGACA GGTGCGCGCA GCGCTCTGG TCAATTTTCG CGAGGACCG TTTCTGCTGA GCGGACGAT GATCGGCCCTG TCGCTTGGG
TAGTACGTT AGCATCCTGT CCACGCGCT CCACGCGCT GCGGAGACC AGTAAAGCC GCTCCTGGG AAAGCGACT CCGCTGCTA CTAGCCGGAC AGCGAACGCC

1601 TATTCGGAAT CTTGCACGCC CTCGCTCAAG CTTCTGTCAC TGGTCCCGC ACCAAACGTT TCGGCGAGAA GCGGCCATT ATCGCCGGCA TGGCGGCCGA
ATAAGCCTTA GAACGTGCGG GAGCGAGTTC GGAAGCAGTG ACCAGGCGG TGGTTTGCA AGCCGCTCTT CGTCCGGTAA TAGCGGCCGT ACCGCCGCT

1701 CGCGCTGGG TAGTCTTGC TGGGCTTGC GACGCGAGG TGGATGGCT TCCCATTTAT GATTTCTTC GCTTCCGGG GCATCGGGAT GCCCGCGTTG
GCGGACCCG ATGAGAACG ACCGCAAGC CTGCGCTCG ACCTACCGA AGGGTAATA CTAAGAAGAG CGAAGGCCG CGTAGCCCTA CCGGCGCAAC

1801 CAGGCCATGC TGTCCAGGCA GGTAGATGAC GACCATCAGG GACAGTTCA AGGATCGCT CCGGCTCTTA CAGCCCTAAC TTCGATCACT GGACCGCTGA
GTCCGGTACG ACAGTCCGT CCATCTACTG CTGGTAGTCC CTGTGAAAT TCCTAGCGG CCGCGAGAA GTTCGGATTG AAGCTAGTGA CCTGGCGACT

1901 TCGTCACGG GATTTATGCC GCCTCGSCGA GCACATGGAA CCGGTTGGCA TGGATTGTAG GCGCGGCCCT ATACCTTGT TGCCTCCCC CGTTGCGTGC
AGCAGTGCCG CTAATACGG CCGAGCGCT CGTGACTT ACCTAACATC CCGCGCGGA TATGGAACAG ACGGAGGGG GCAACGCGAG

2001 CCGTGCAATG AGCGGGCCA CCGGACCTG AATGGAAGC TACCTTCGG CCGCGCTGGA GCGATTGCTT AAGTGTGAG GTTCTTAACC TCGGTTAGTT AAGAAGCCT
GCCACGTACC TCGGCGCGGT GGAGCTGGAC

2101 GAACTGTGAA TCGGCAAAACC AACCTTGGC AGAACAATC CATCGCTCC GCCATCTCCA GCAGCGCAC GCGCGCATC TCGGGCAGG TTGGTCTCTG
CTTGACACTT ACGCGTTGG TTGGGAACCG TCTGTATAG GTAGCGCAGG CCGTAGAGGT CCGCGCGTG CCGCGCTAG AGCCGCTCG AACCAGGAC

2201 GCCACGGGTG CGCATGATCG TGCTCTCTG GTTGAGGACC CCACTCTTG GCCGATCCGA CCGCCCCAAC GGAATGACCA ATCGTCTTAC TTAGTGGCTA TGGCTCGCT
CGGTGCCCC GCGTACTAGC ACGAGGACAG CAATCTCTG CCGGATCCGA CCGCCCCAAC GGAATGACCA ATCGTCTTAC TTAGTGGCTA TGGCTCGCT

2301 ACGTGAAGCG ACTGCTGCTG CAAACGCTT CCGACCTGAG CCGCTGACTC GTTGTGTAC TTACCAGAAG CCAAGGCAC AAAGCATTC AGACCTTTGC GCGTTCAGTC
TGCACTTGC TGACGACGAC GTTTTGACA GTTTTGACA CCGCTGACTC GTTGTGTAC TTACCAGAAG CCAAGGCAC AAAGCATTC AGACCTTTGC GCGTTCAGTC

2401 CGCCCTGCAC CATTATGTT CCGATCTGCA TCGCAGGATG CCGTGTGGA CCCTGTGGA CACTTACATC TGTATTAACG AAGCGTGGC ATTGACCCCTG
GCGGACGCTG GTATATACAG GCCTAGACGT ACGTCTCTAC GACGACCGAT GGGACACCTT GTGGATGTAG ACATAATTG TCGCGGACCG TAACTGGGAC

FIG. 3B

2501 AGTGATTTT CTCTGGTCC GCGCATCCA TACGCCAGT TGTTTACCT CACAACGTT CAGTAACCG GCATGTTCT CATCAGTAAC CCGTATCGTG
TCACTAAAA GAGACCAGG CGCGTAGGT ATGGCGGTCA ACAATGGGA GTGTTGCAAG GTCAATGGCC CGTACAAGTA GTAGTCATTG GGCATAGCAC

2601 AGCATCCTCT CTCGTTTCAT CCGTATCAT ACCCCCATGA ACAGAAATTC CCCCTTACAC GGAGGCATCA AGTGACCAAA CAGGAAAAAA CCGCCCTTAA
TCGTAGSAGA GAGCAAAGTA GCCATAGTAA TGGGGTACT TGTCTTTAAG GGGGAATGT CCTCCGTAGT TCACTGGTTT GTCCCTTTT GGCGGGAATT

2701 CATGGCCGC TTTATCAGAA GCCAGACATT AACGTTCTG GAGAAACTCA ACAGAGTGA CGCGATGAA CCGGTCTGT GTCCGTCTGT GCTTACAGC
GTACCGGCGG AATAGTCTT CCGTCTGTAA TTGCGAAGAC CTCTTTGAGT TGCTCGACCT GCGCTACTT GTCCGTCTGT AGACACTTAG CGAAGTGTG

2801 CACGCTGATG AGCTTTACCG CAGCTGCCTC GCGGTTTCG GTGATGACGG TGAAAACTC TGACACATGC AGCTCCCGA GACGCTCACA GCTTGTCTGT
GTGCGACTAC TCGAAATGGC GTCGACGGAG CGCGAAAGC CACTACTGCC ACTTTGGAG ACTGTGTAG TCGAGGGCCT CTGCCAGTGT CGAACAGACA

2901 AAGCGGATGC CCGGAGCAGA CAAGCCCGTC AGGCGCGTC AGCGGTGTT GCGGGGTGTC GGGCGGAGC CATGACCCAG TCACGTAGCG ATAGCGGAGT
TTGCGCTACG GCCCTCGTCT GTTCGGGCAG TCCCGCGCAG TCGCCACAA CCGCCACAG CCGCGGTG GTACTGGTC AGTGATCGC TATCGCCTCA

3001 GTATACTGC TTAACATATG GGCATCAGAG CAGATTGTAC TGAGAGTGCA CCATATGCGG TGTGAAATAC CGCACAGATG CGTAAGGAGA AAATACCGCA
CATATGACCG AATTGATACG CCGTAGTCTC GTCTAACATG ACTCTACGT GGTATACGCC ACACCTTTATG CCGTGTCTAC GCATTCTCT TTTATGGCGT

3101 TCAGCGGCTC TTCGCTTCC TCGCTCACTG ACTCGTGGG CTGCGTCTGTT CCGCTGCGG GAGCGGTATC AGCTCACTCA AAGCGGTAA TACGGTTATC
AGTCCCGGAG AAGCGAAGG AGCGAGTAC TGAGCGACGC GAGCCAGCAA GCCGACCGG CTCGCCATAG TCGAGTGTG TTCCGCCATT ATGCCAATAG

3201 CACAGAAATCA GGGATAACG CAGGAAAGAA CATGTAGCA AAAGGCCAGC AAAGCGTAA AAGCGCGCT TGCTGGCGT TTTCCATAGG
GTGCTTGTAGT CCCCTATTGC GTCCCTTCTT GTACACTCGT TTTCCGGTGC TTTTCCGGTC CTTGGCATT TTCCGGCGCA ACGACCGCAA AAAGGTATCC

3301 CTCGCGCCCC CTGACGAGCA TCACAAAAAT CGACGCTCAA GTCAGAGGTG GCGAAACCCG ACAGGACTAT AAAGATACCA GCGCTTTCCC CCTGGAAGCT
GAGCGGGGG GACTGCTCGT AGTGTTTTAA GCTGCGAGTT CAGTCTCCAC CGCTTTGGG TGTCTGATA TTCTATGTT CCGCAAAGG GACCTTCGA

3401 CCCTCGTGG CTCTCCTGTT CCGACCCCTGC CGCTTACCG ATACCTGTCC GCCTTTCTCC CTTCCGGGAG CTTGGCGCTT TCTCATAGCT CACGCTGTAG
GGGAGCACGC GAGAGGACAA GGCTGGGACG GCGAATGGCC TATGGACAGG CGGAAAGAGG GAAGCCCTTC GCACCGCGAA AGAGTATCGA GTGCGACATC

3501 GTATCTCAGT TCGGTGTAGG TCGTTCGCTC CAAGCTGGG TGTGTGACG AACCCCGCT TCAGCCCGAC CGCTGCGCCT TATCCGGTAA CTATCGTCTT
CATAGAGTCA AGCCACATCC AGCAAGCGAG GTTCGACCCG ACACACGTGC TTGGGGGCA AGTCGGGCTG GCGACCGGA ATAGGCCATT GATAGCAGAA

3601 GAGTCCAACC CCGTAAGACA CGACTTATCG CCACTGGCAG CAGCCACTGG TAACAGGATT AGCAGAGCGA GGTATGTAGG CCGTGTCTACA GAGTTCTTGA
CTCAGGTTGG GCCATTCTGT GTGAATAGC GGTGACCGTC GTGCTGTGACC ATTGTCTTAA TCGTCTCGCT CCATACATCC GCCACGATGT CTCAAGAACT

3701 AGTGGTGGC TAACTACGGC TACACTAGAA GGACAGTATT TGGTATCTGC GCTCTGTGA AGCCAGTTAC AGCCGAAA AGAGTTGTA GCTCTTGATC
TCACCACCGG ATTGATGCC ATGTGATCTT CCTGTCTATA ACCATAGACG CGAGACGACT TCGGTCAATG GAAGCCTTTT TCTCAACCAT CGAGAACTAG

FIG. 3C



3801 CGGCAACAA ACCACCGCTG GTAGCGGTGG TTTTCTTGTG TGCAAGCAGC AGATTACGGC CAGAAAAAA GGATCTCAAG AAGATCCTTT GATCTTTTCT
GCCGTTTGT TGGTGGCGAC CATCGCCACC AAAAAACAA ACGTTCTGTC TCTAATGCGC GTCCTTTTCT CCTAGAGTTC TTCTAGGAAA CTAGAAAAA
3901 ACGGGGCTG ACGCTCAGTG GAACGAAAA TCACGTTAAG GGATTTTGGT CATGAGATTA TCAAAAAGGA TCTTCACCTA GATCCTTTTA AATTAAAAA
TGCCCCAGAC TCGAGTGCAC CTTGCTTTTG AGTGCAATTC CCTAAAACCA GTACTCTAAT AGTTTTCCT AGAAGTGGAT CTAGAAAAA TTAATTTTA
4001 GAAGTTTAA ATCAATCTAA AGTATATATG AGTAACTTG GTCTGACAGT TACCAATGCT TAATCAGTGA GGCACCTATC TCAGCGATCT GTCTATTTCG
CTTCAAAAT TAGTTAGATT TCATATATAC TCATTTGAC CAGACTGTCA ATGGTTACGA ATTAGTCACT CCGTGGATAG AGTCGTAGA CAGATAAAGC
4101 TTCATCCATA GTTGCTGAC TCCCCGTCGT GTAGATAACT ACGATACGGG AGGCTTACC ATCTGGCCC AGTGCTGCAA TGATACCGG AGACCCACGC
AAGTAGGTAT CAACGGACTG AGGGGCAGCA CATCTATTGA TGCTATGCC TCCCGAATGG TAGACCGGG TCACGACGTT ACTATGGCGC TCTGGGTGCG
4201 TCACCGGCTC CAGATTTATC ACCAATAAC CAGCCAGCCG GAAGGGCCGA GCGCAGAAGT GGTCTGCAA CTTTATCCGC CTCCATCCAG TCTATTAAAT
AGTGGCCGAG GTCTAAATAG TCGTTATTG TCGGTCGCGC CTTCCCGCT CCGCTCTCA CCAGGACGTT GAAATAGGCG GAGGTAGGTC AGATAATTAA
4301 GTTGCCGGA AGCTAGAGTA AGTAGTTCG CAGTTAATAG TTTGCGCAAC GTTGTGCCA TTGCTGCAGG CATCGTGGTG TCACGCTCGT CGTTTGGTAT
CAACGGCCCT TCGATCTCAT TCATCAAGCG GTCAATTATC AAACGCGTTG CAACAACGGT AACGACGTC GTAGCACAC AGTGCGAGCA GCAAACCAT
4401 GGCTTCATC AGCTCCGCTT CCCAACGATC AAGCGGAGT ACATGATCCC CCATGTTGTG CAAAAAGCG GTTAGCTCCT TCGGTCTCC GATCGTTGTC
CCGAAGTAAG TCGAGGCCAA GGGTTGCTAG TTCCGCTCAA TGACTAGG GGTACACAC GTTTTTTCG CAATCGAGGA AGCCAGGAG CTAGCAACAG
4501 AGAAGTAAGT TGGCCGAGT GTATCACTC ATGGTTATGG CAGCACTGCA TAATCTCTT ACTGTCAATG CATCCGTAAG ATGCTTTTCT GTGACTGGTG
TCTTCATTCA ACCGGCGTCA CAATAGTGAG TACCAATACC GTCGTGACGT ATTAAGAGAA TGACAGTACG GTAGGCATTC TACGAAAAA CACTGACCAC
4601 AGTACTCAAC CAAGTCATTC TGAGATAGT GTATGCGCGG ACCGAGTTGC TCTTGCCCGG CGTCAACACG GGATAATACC GCGCCACATA GCAGAACTTT
TCATGAGTTG GTTCAGTAAG ACTCTATCA CATAAGCCGC TGCTCAACG AGAACGGGC GCAAGTTGTC CCTATTATGG CCGGTGTAT CGTCTTGAAA
4701 AAAAGTGCTC ATCATTTGAA AACGTTCTTC GGGGCGAAA CTCTCAAGGA TCTTACCGCT GTTGAGATCC AGTTCGATGT AACCCACTCG TGCACCCCAAC
TTTTACAGG TAGTAACCTT TTGCAAGAG CCCCCTTTT GAGAGTCTCT AGAATGGCGA CAACTCTAGG TCAAGCTACA TTGGGTGAGC ACGTGGGTG
4801 TGATCTTCAG CATCTTTTAC TTTCACCAGC GTTCTGCGT GAGCAAAAA GAGAAAGCAA AATGCCGCAA AAAAGGGAAT AAGGGCGACA CGGAAATGTT
ACTAGAAGTC GTAGAAAATG AAAGTGCTG CAAAGACCCA CTCGTTTTG TCCTTCCGTT TTACGGCGTT TTTCCCTTA TTCCCGCTGT GCCTTTACAA
4901 GAATACTCAT ACTCTTCTT TTTCAATATT ATTGAAGCAT TTATCAGGGT TATTGCTCA TGAGCGGATA CATATTGAA TGTATTTAGA AAAATAAACA
CTTATGAGTA TGAGAGGAA AAAGTTATAA TAACCTCGTA AATAGTCCCA AATACAGAGT ACTCGCCTAT GTATAAACTT ACATAAATCT TTTTATTGT
5001 AATAGGGGT CCGCGACAT TTCCCCGAAA AGTGCCACCT GACGTCTAAG AAACCAATTAT TATCATGACA TTAACCTATA AAAATAGGCG TATCAGGAG
TTATCCCCAA GCGCGTGTA AAGGGCTTT TCACGGTGGA CTGAGATTC TTTGGTAATA ATAGTACTGT AATTGGATAT TTTTATCCGC ATAGTGTCTC
5101 CCCTTTCGTC TTCAA
GGAAAGCAG AAGTT

FIG. 3D

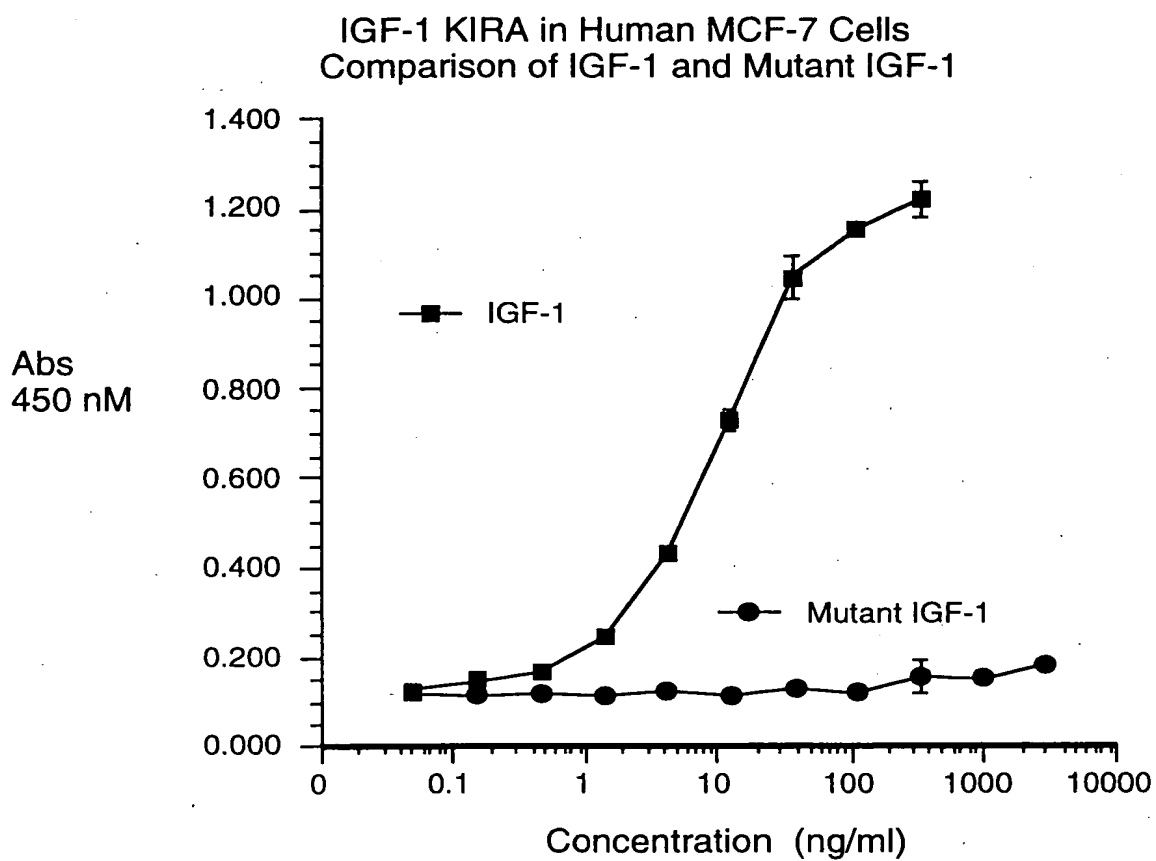
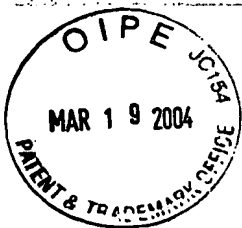


FIG. 4



IGF-1 (Leu²⁴ Ala³¹) is Inactive In Vitro

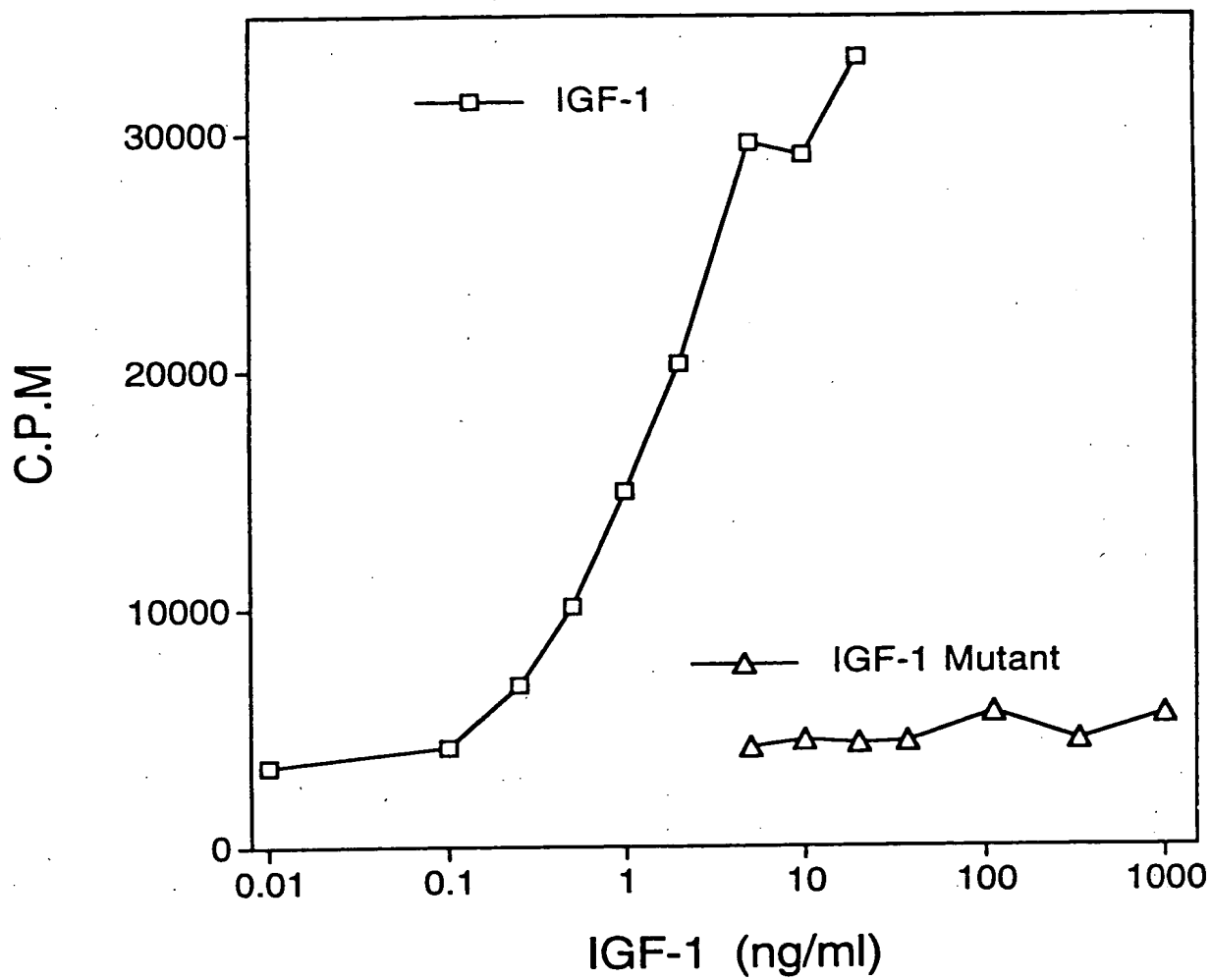


FIG. 5

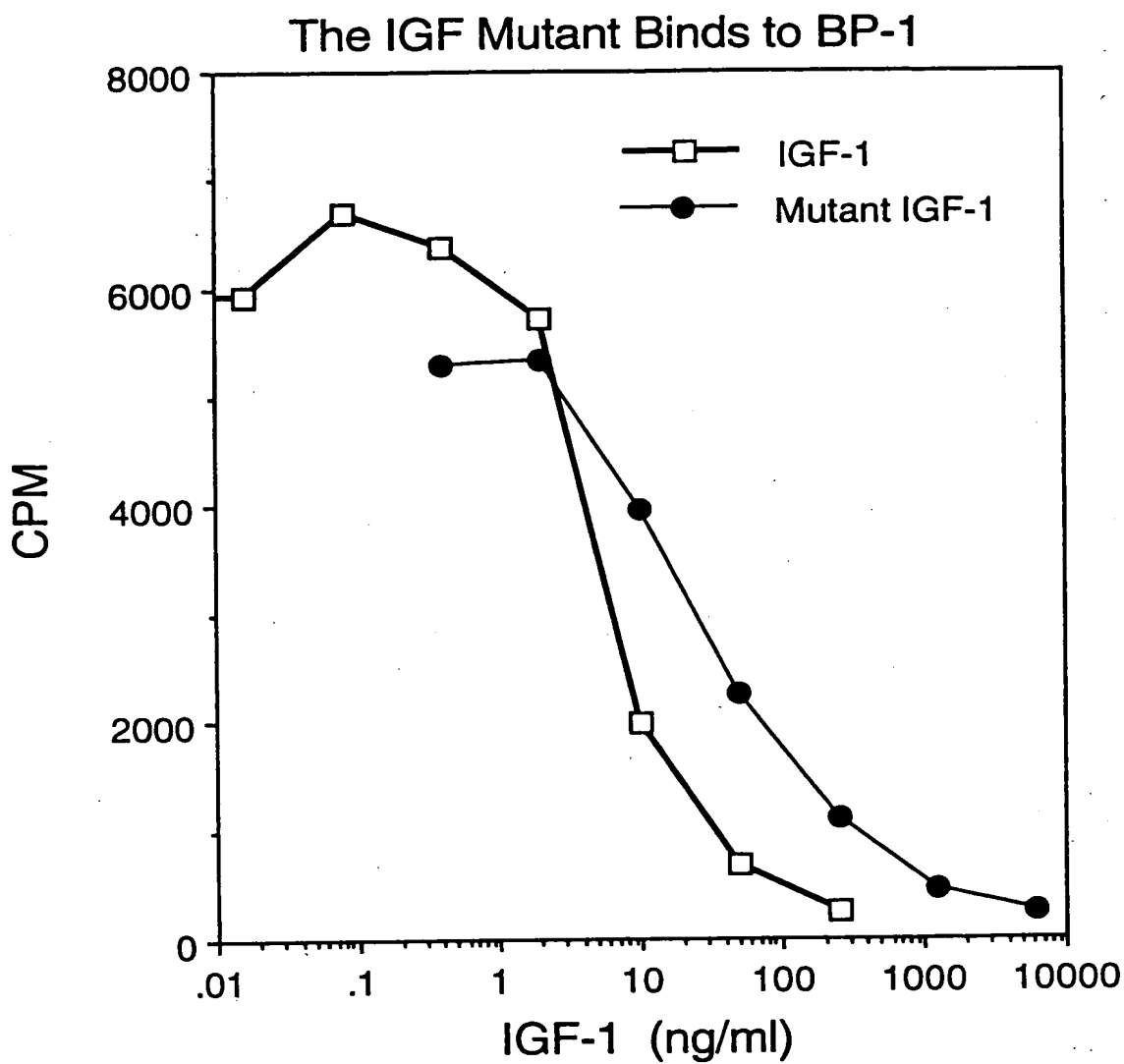


FIG. 6

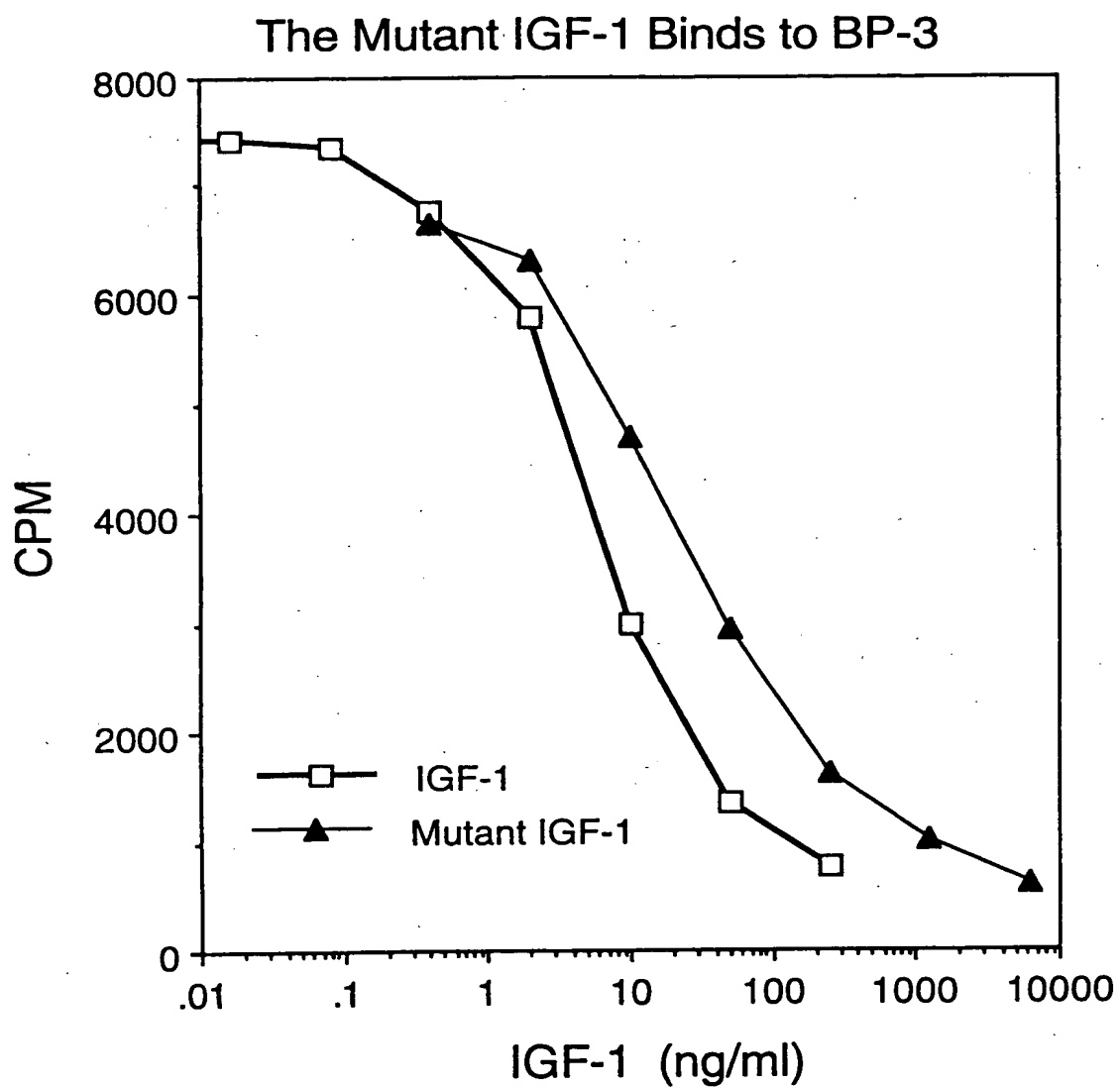
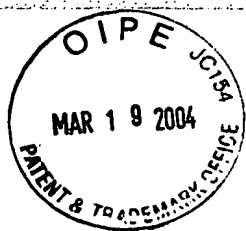


FIG. 7

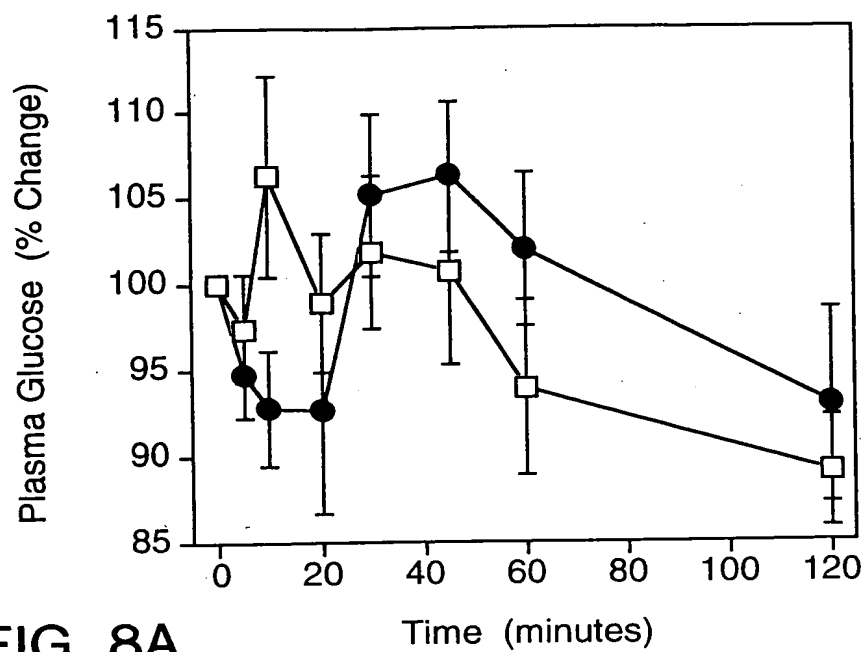
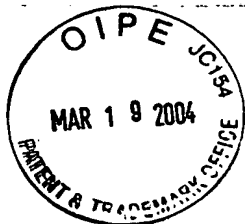


FIG. 8A

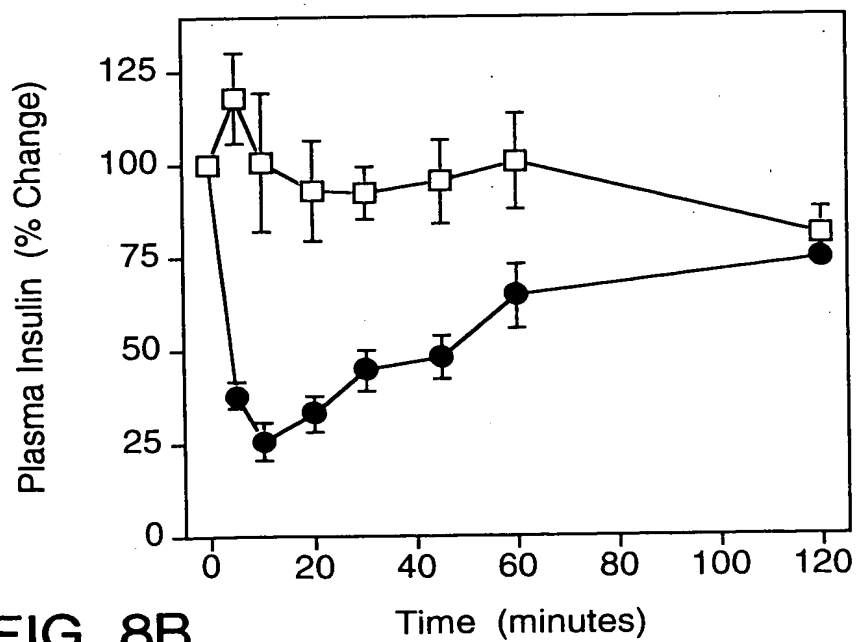


FIG. 8B

—□— Control —●— IGF-Mutant

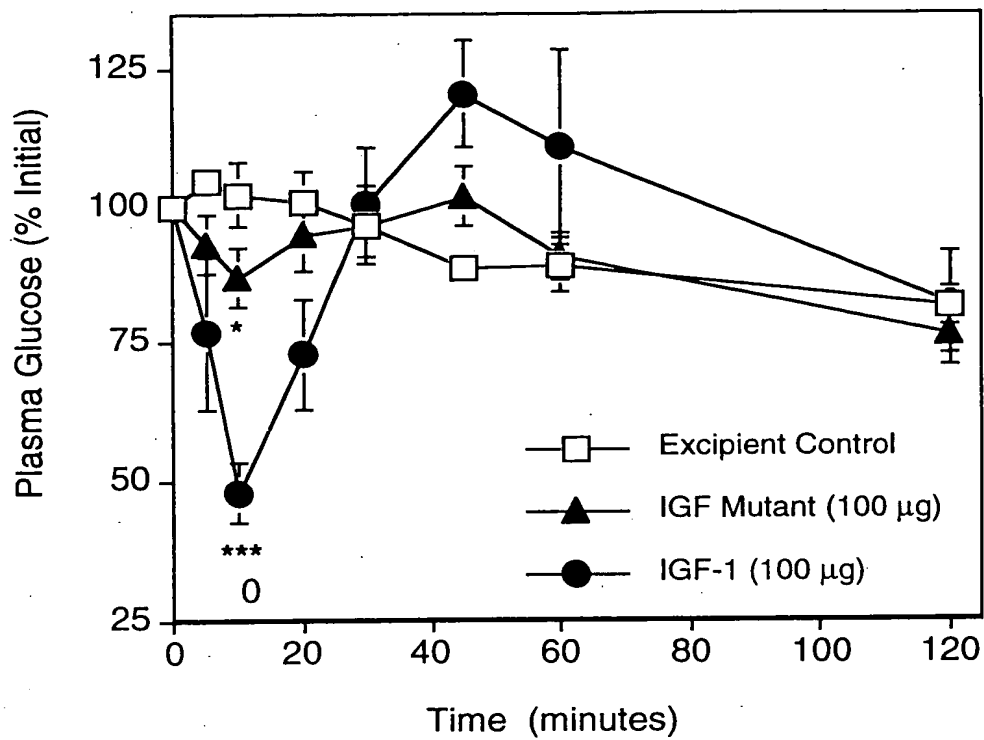


FIG. 9A

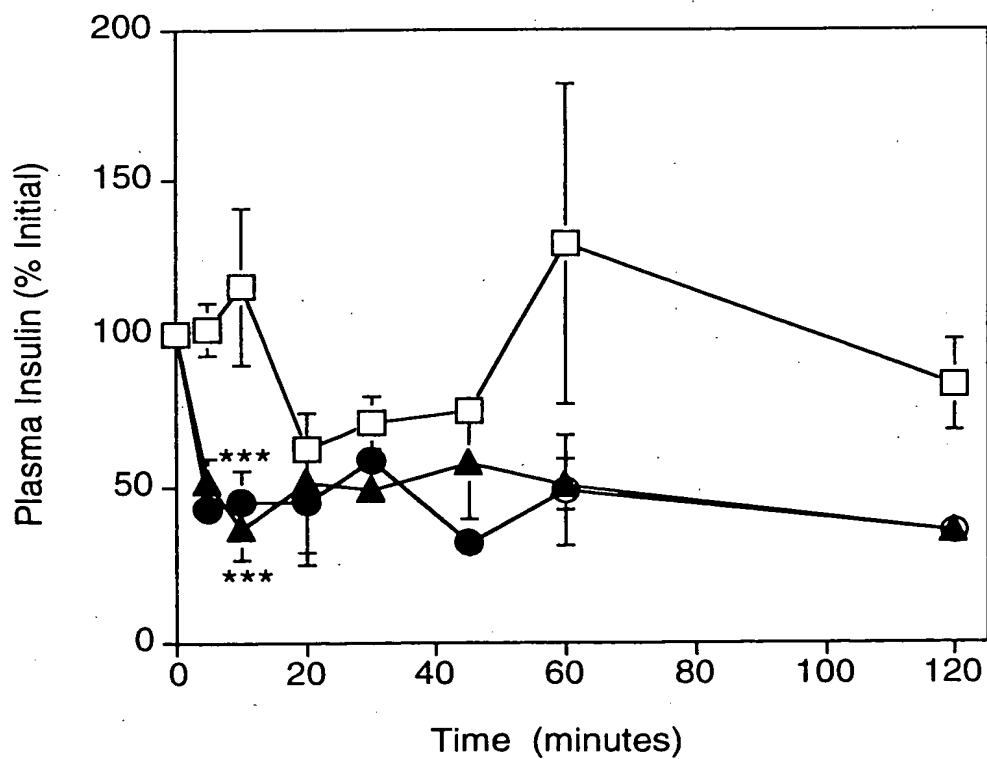


FIG. 9B

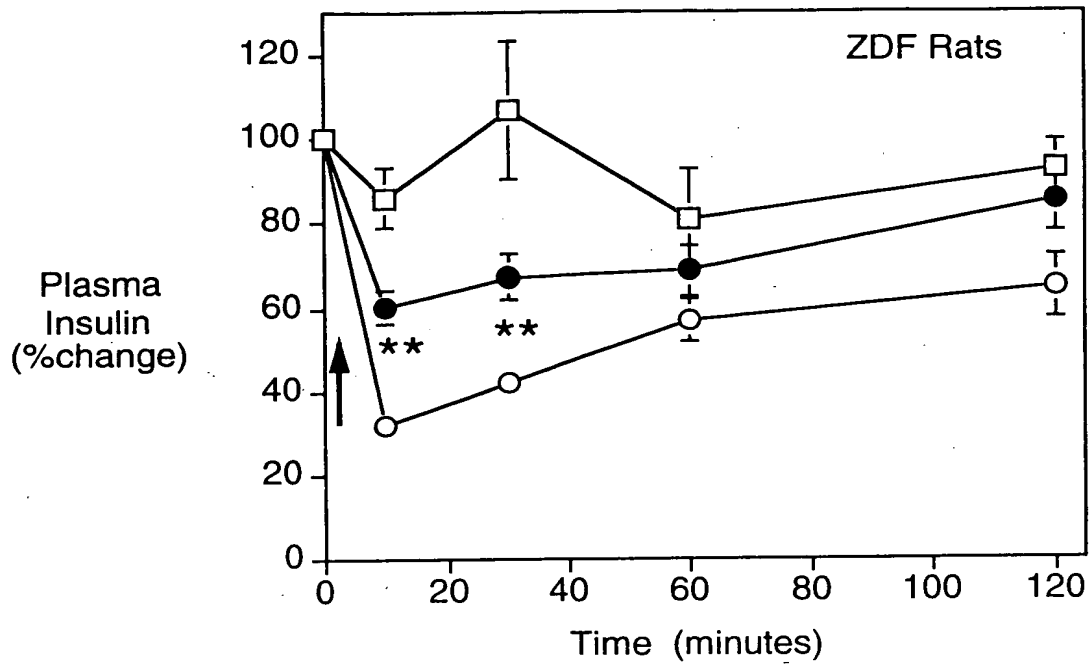


FIG. 10A

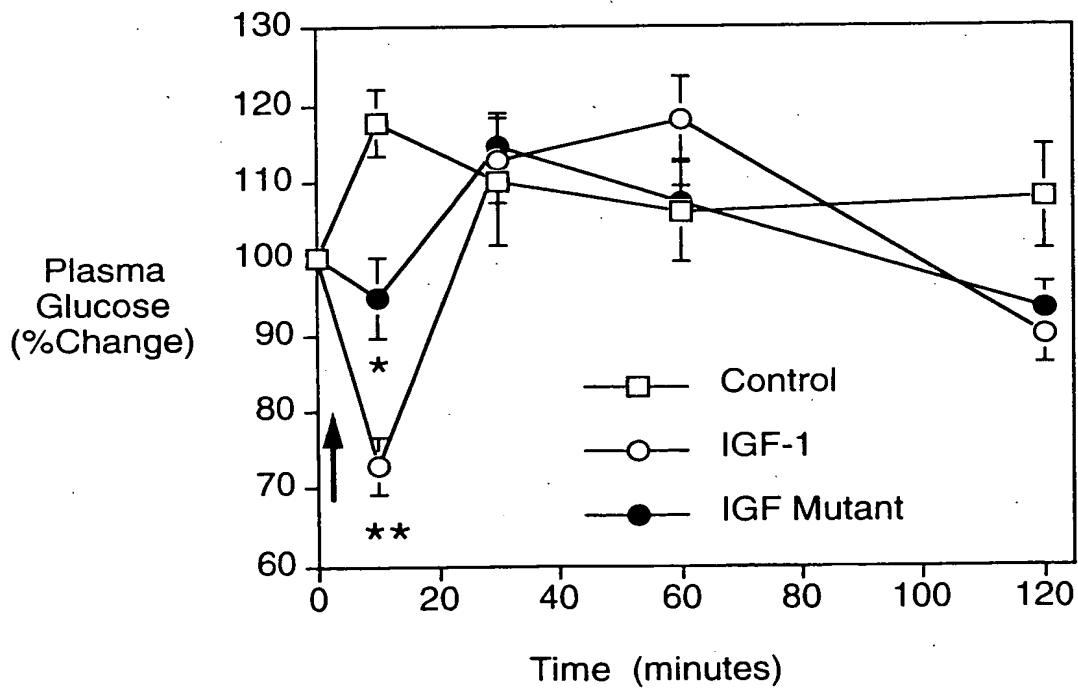


FIG. 10B

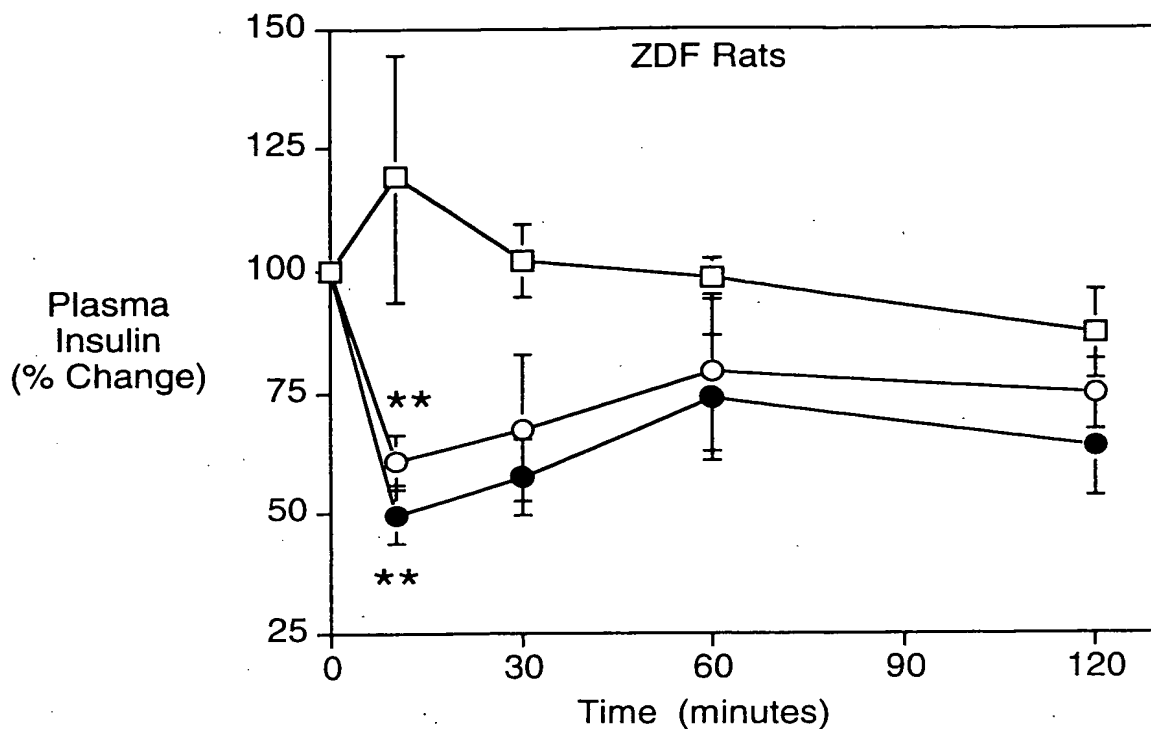


FIG. 11A

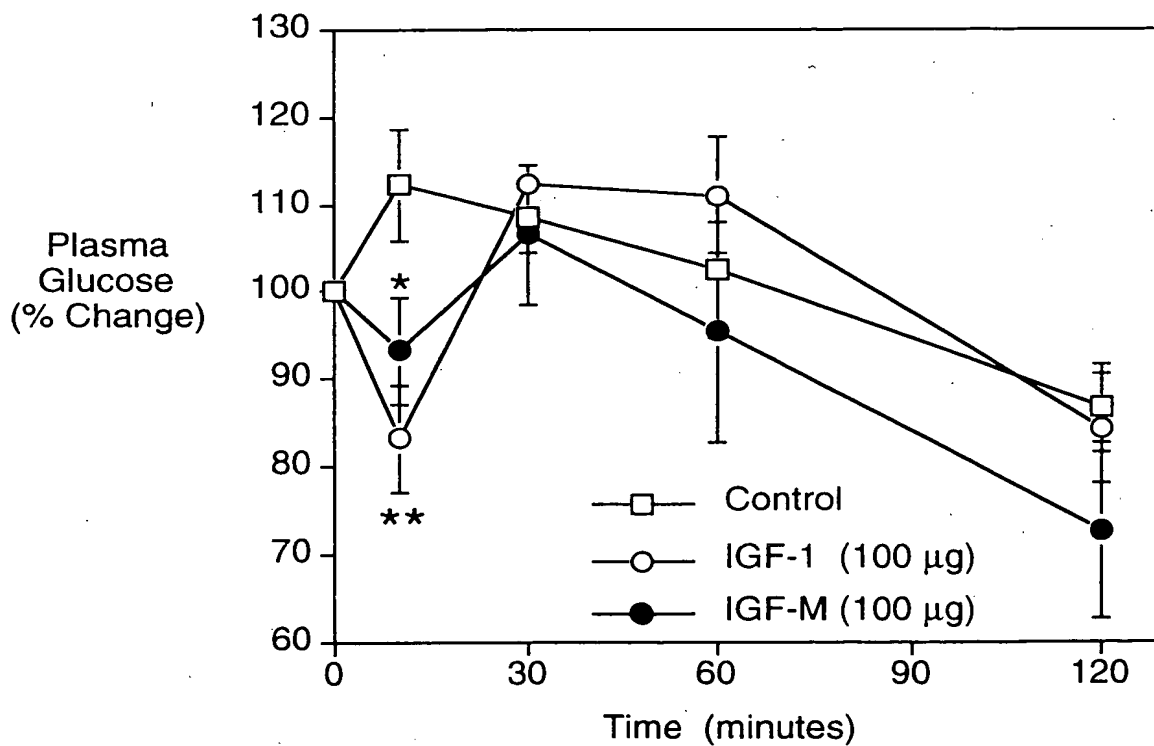


FIG. 11B

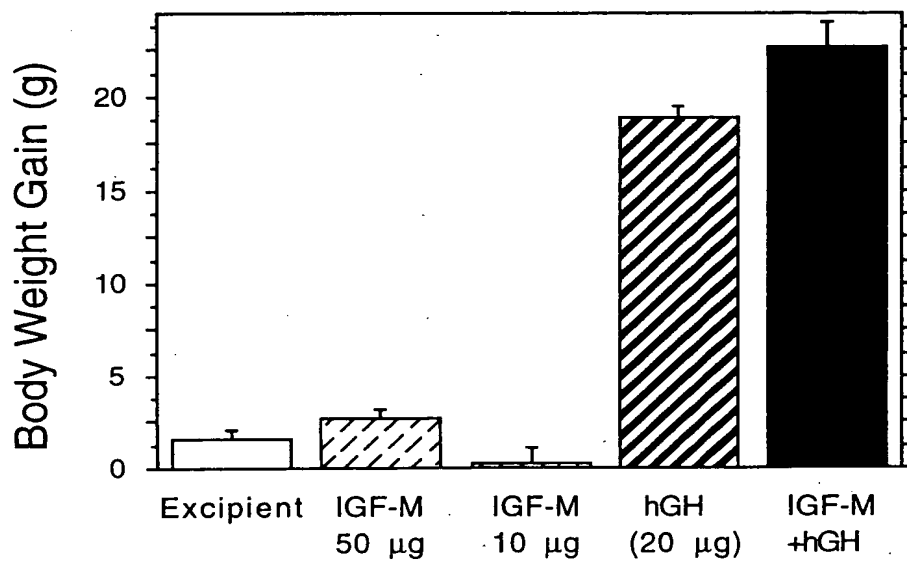


FIG. 12

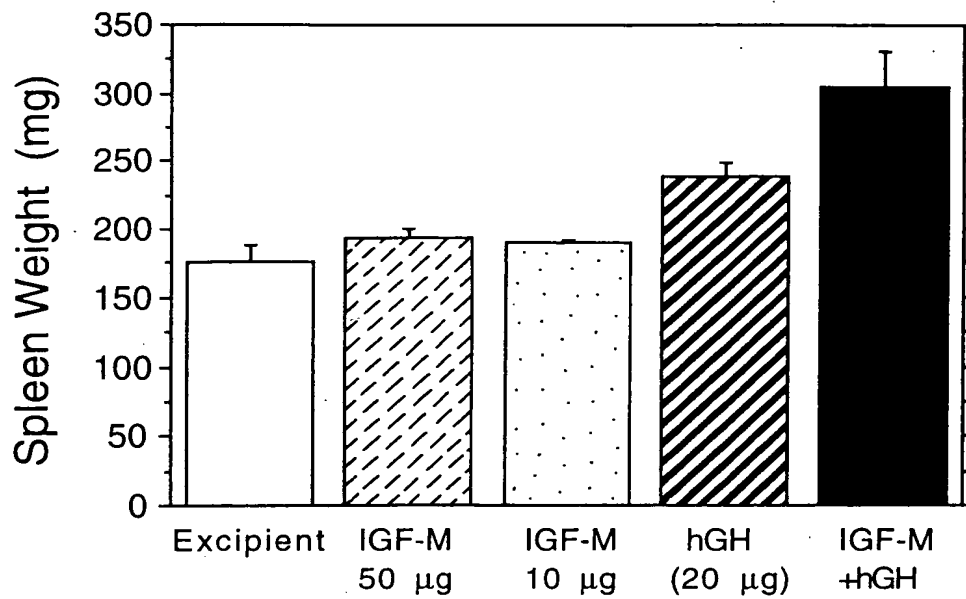


FIG. 13A

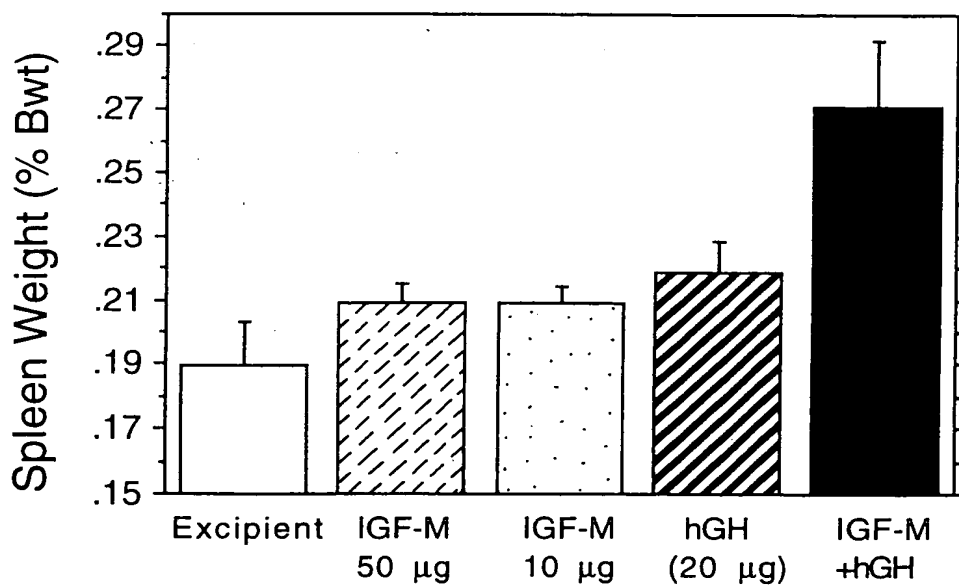


FIG. 13B

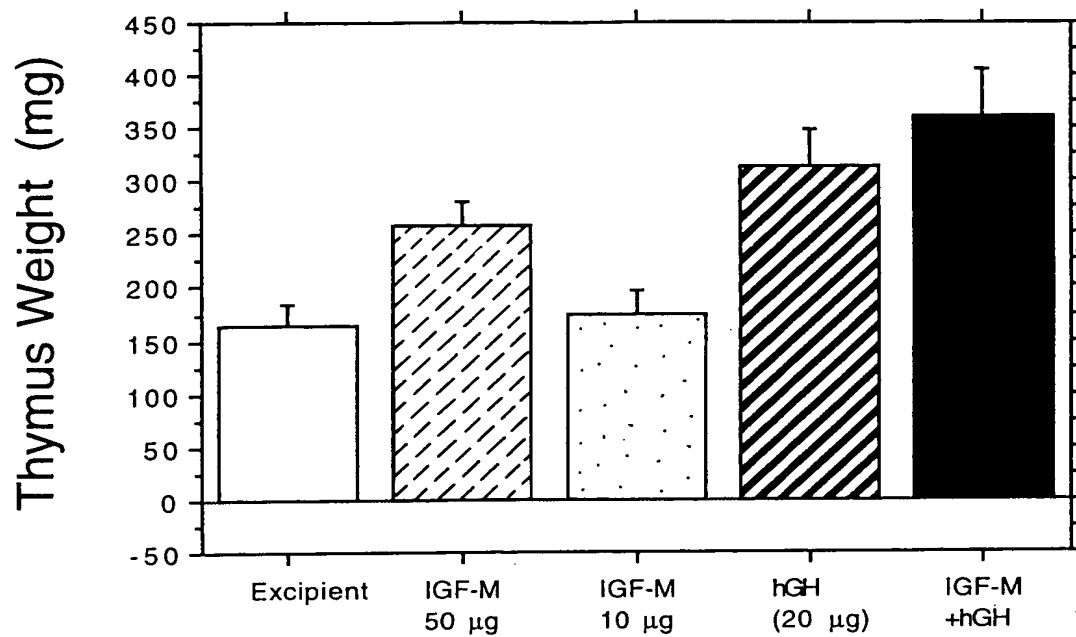


FIG. 14A

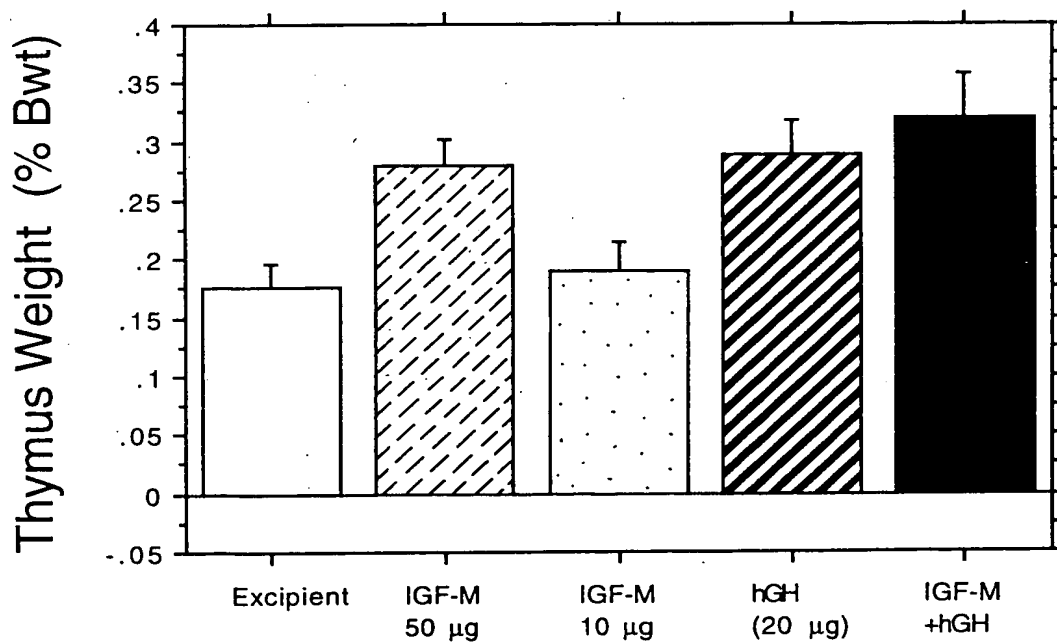


FIG. 14B

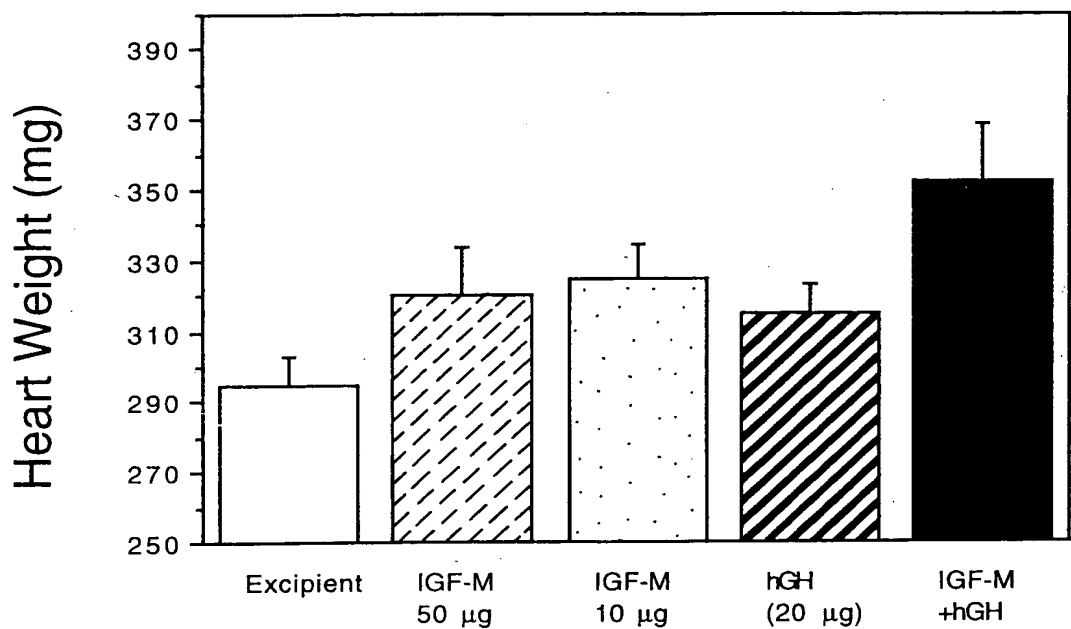


FIG. 15A

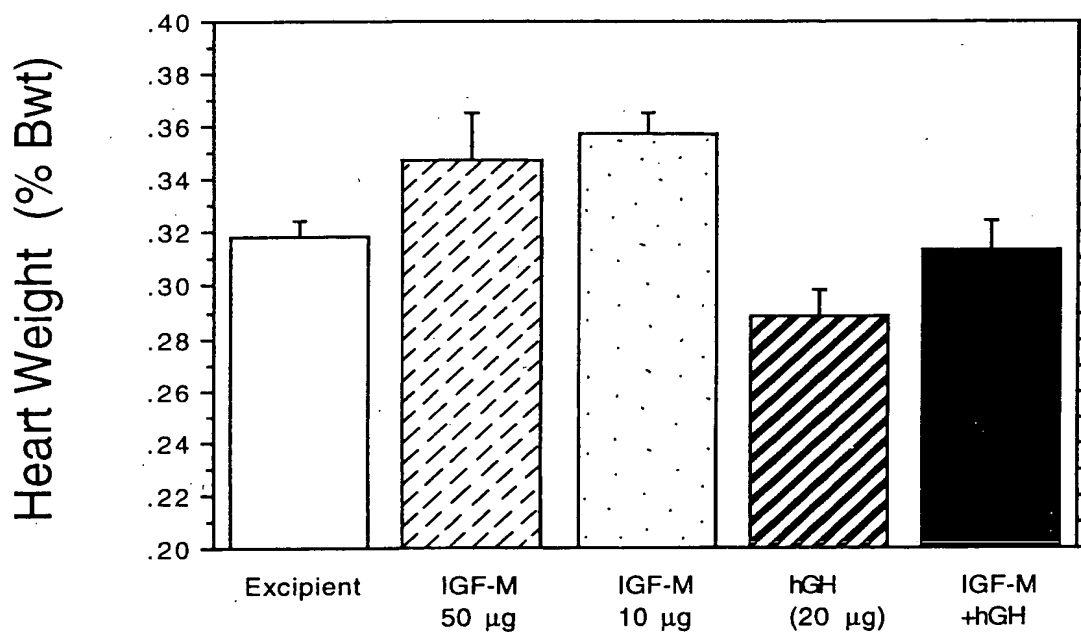


FIG. 15B

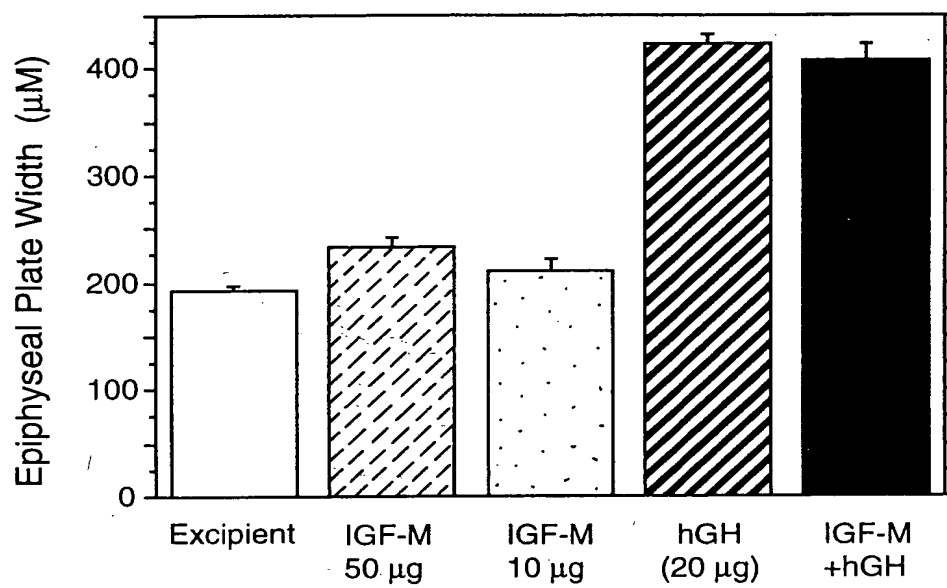


FIG. 16

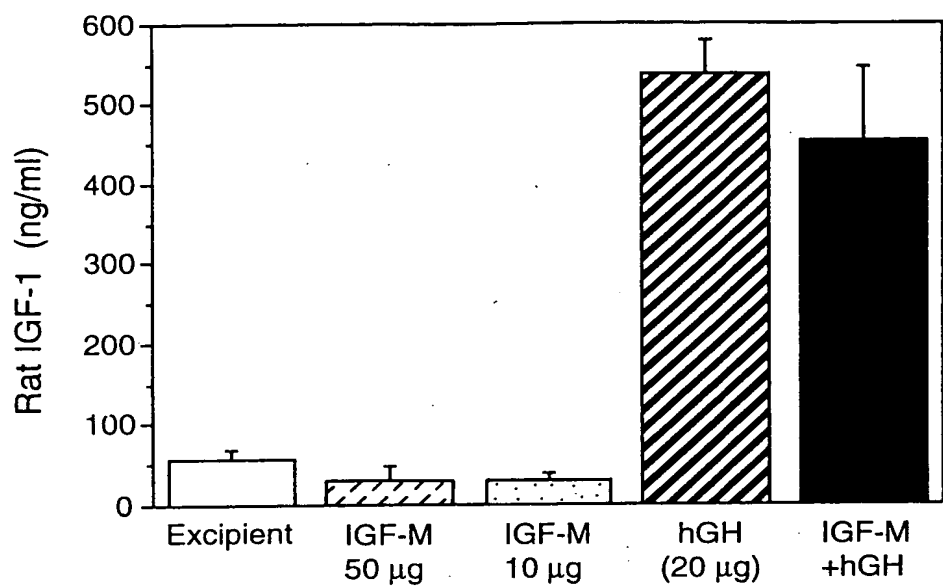


FIG. 17A

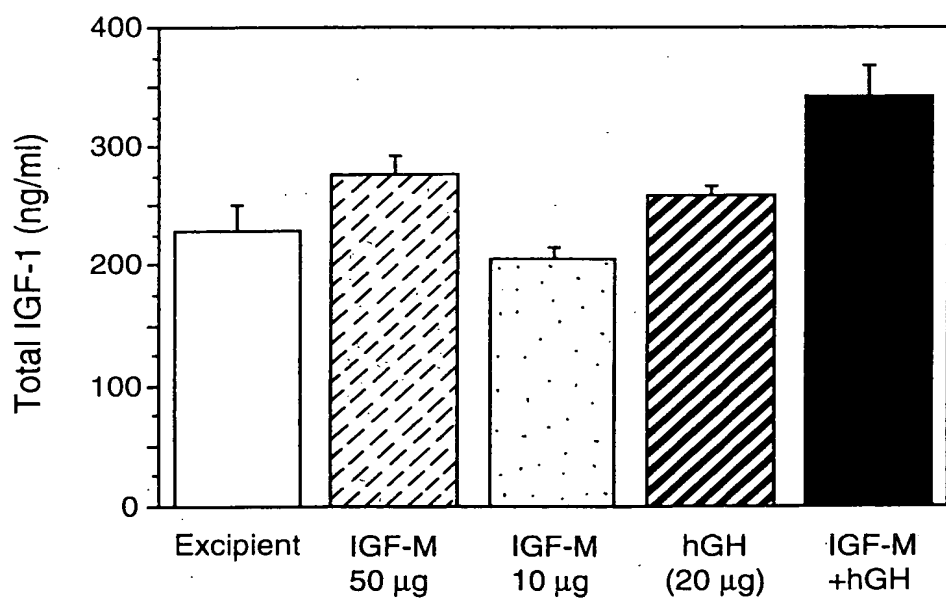


FIG. 17B

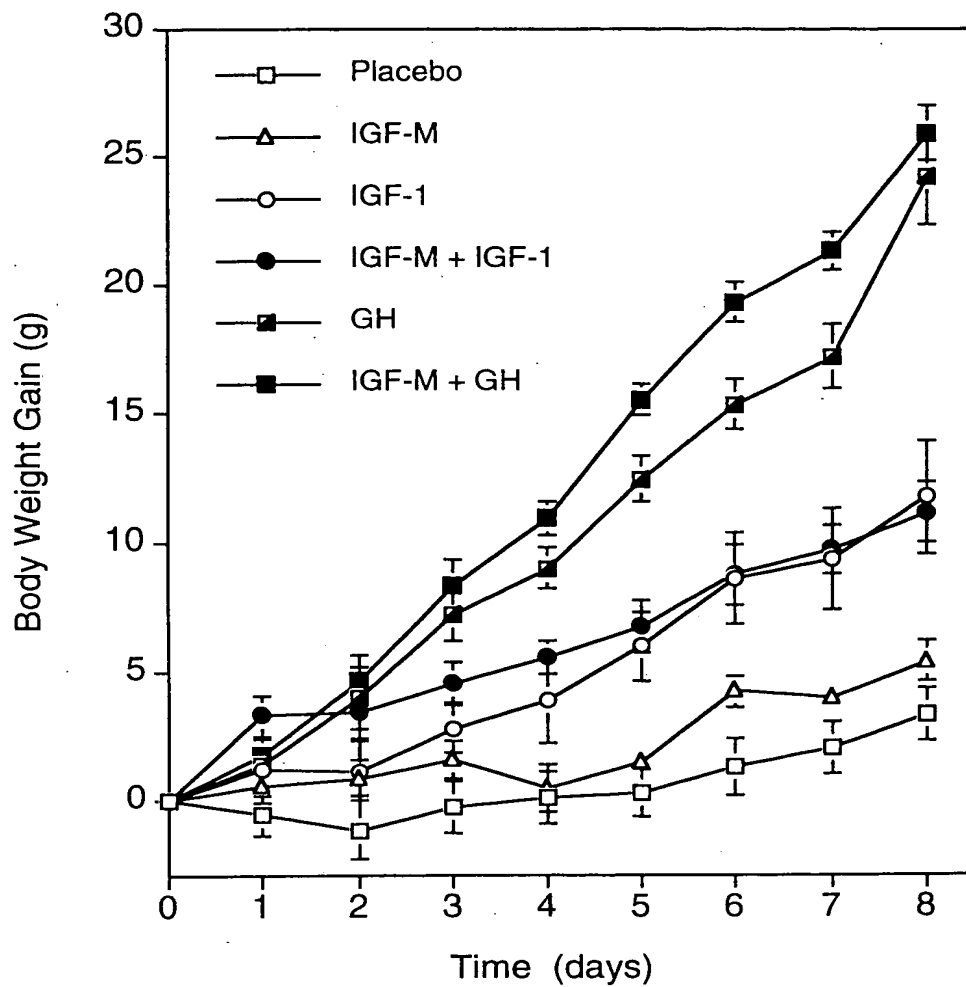


FIG. 18

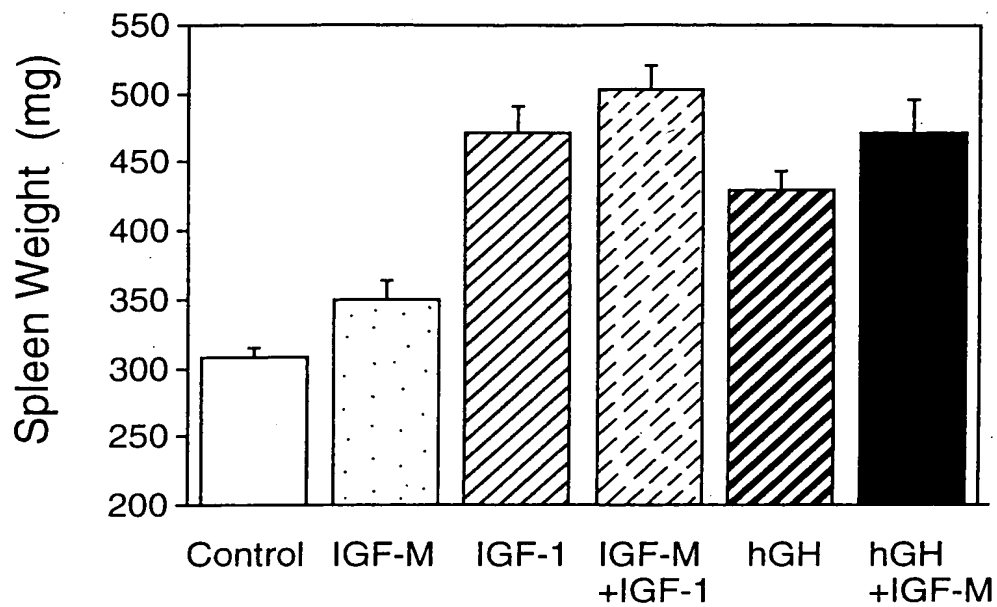


FIG. 19A

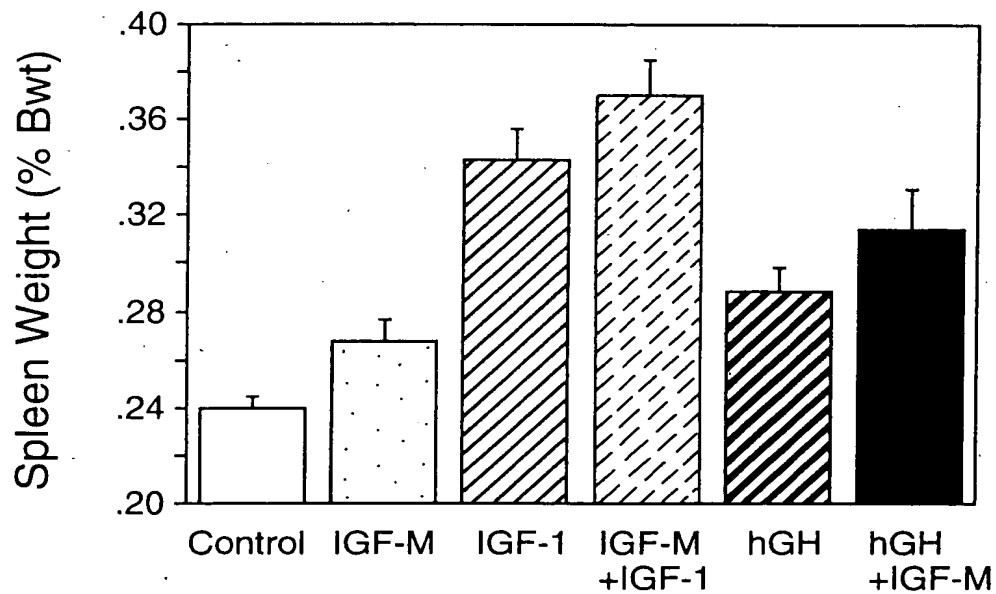


FIG. 19B

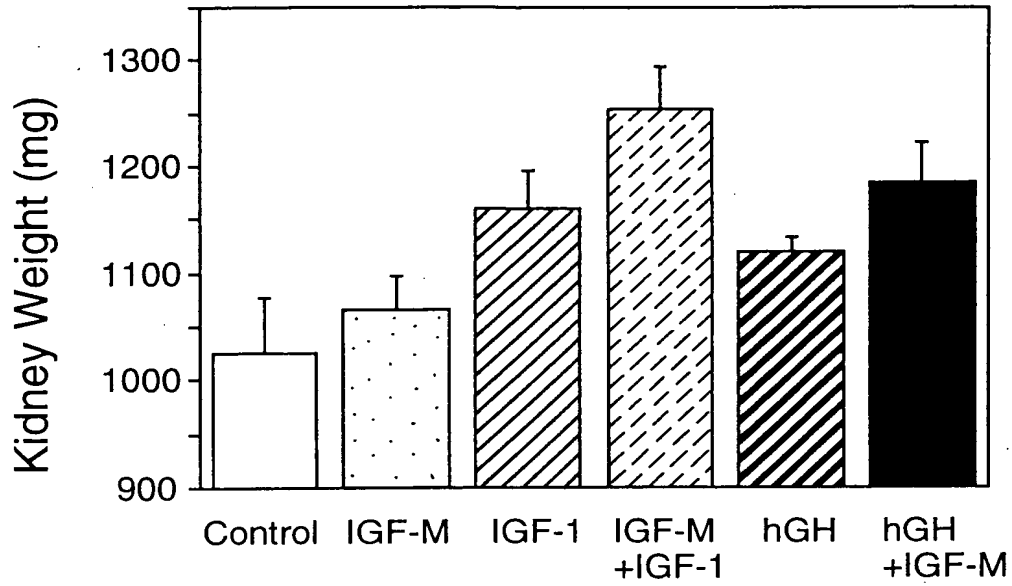


FIG. 20A

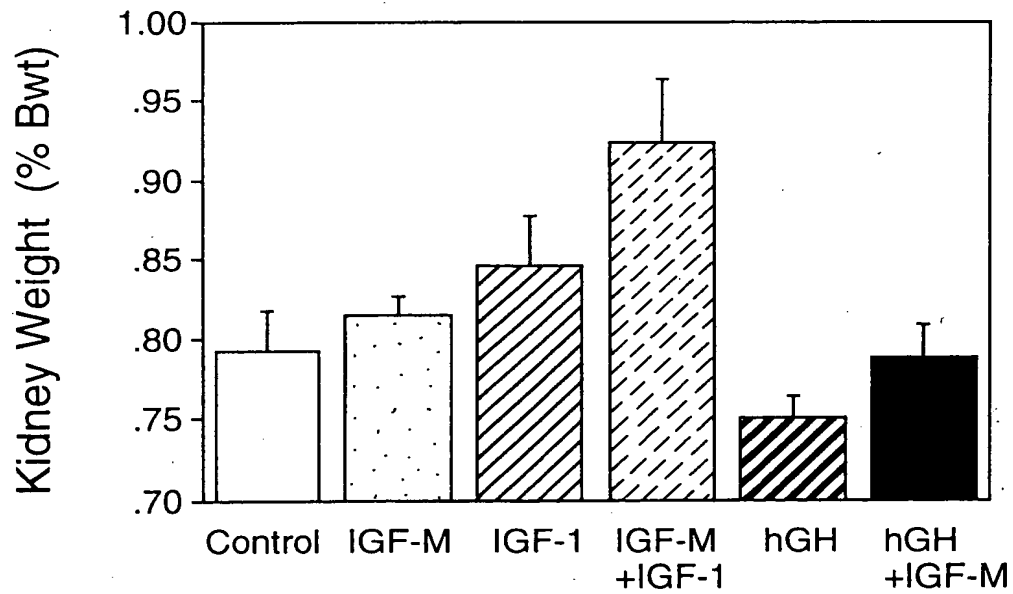


FIG. 20B

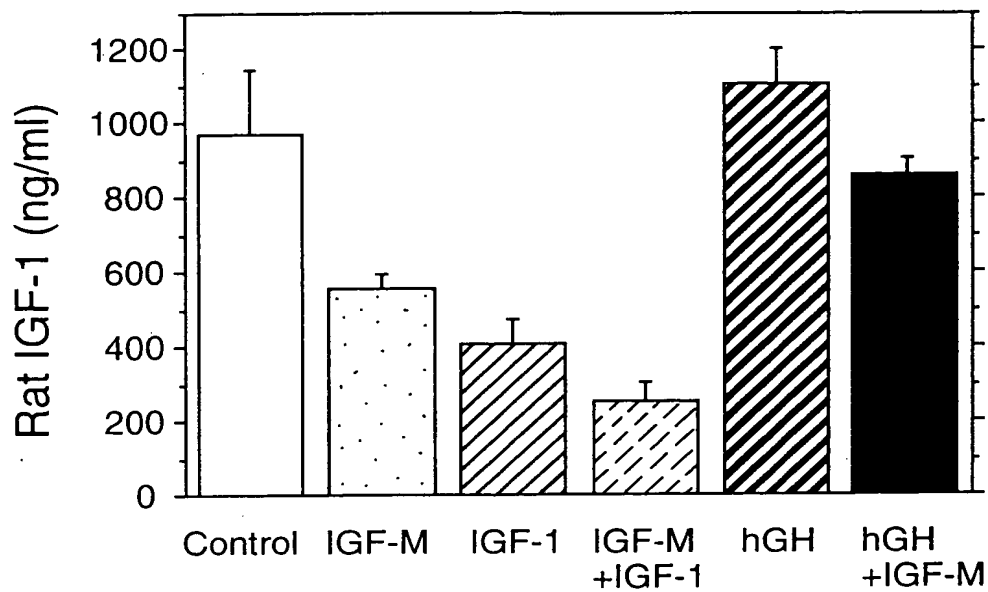


FIG. 21A

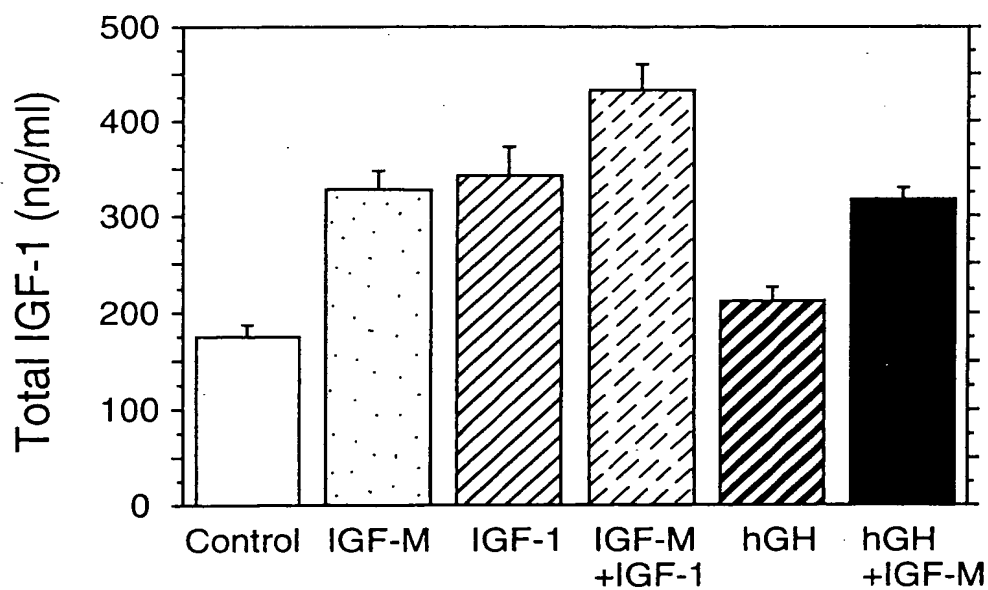


FIG. 21B

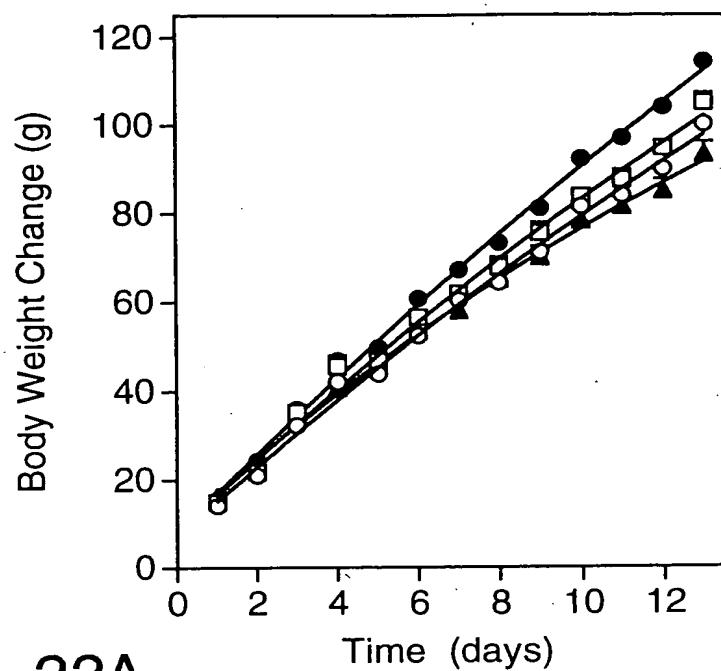


FIG. 22A

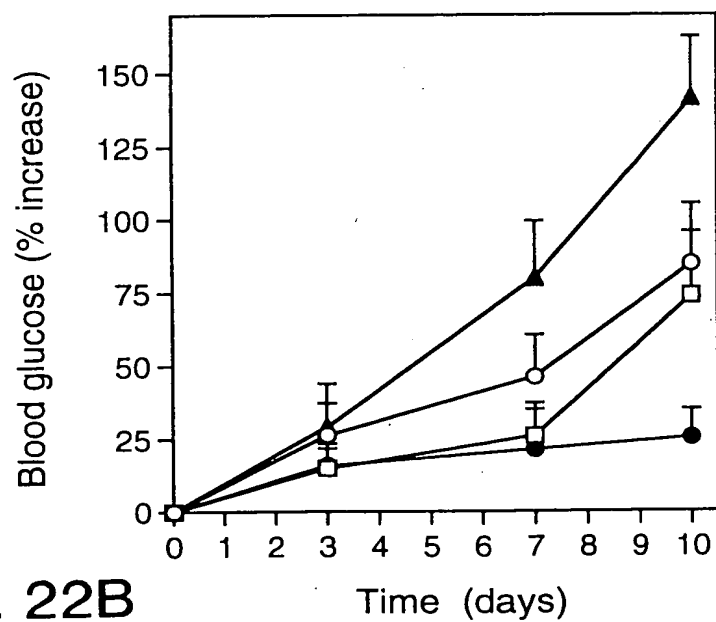
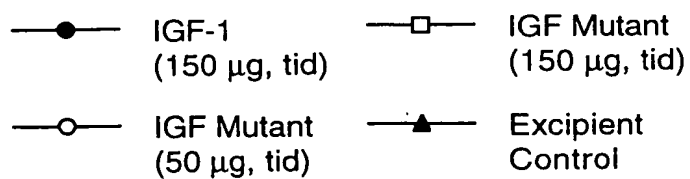


FIG. 22B



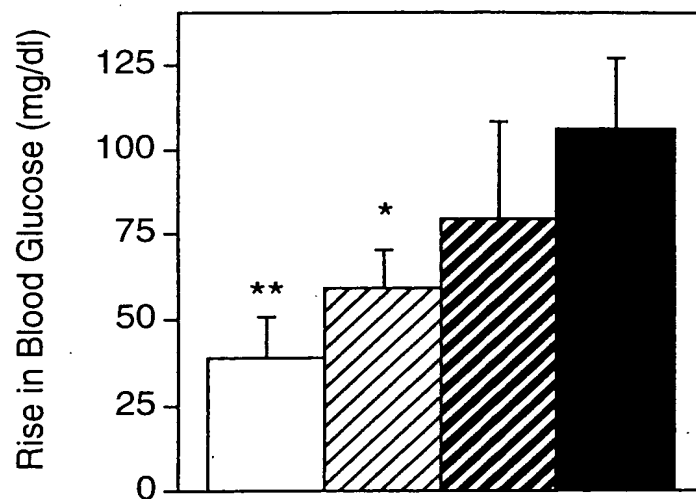


FIG. 23A

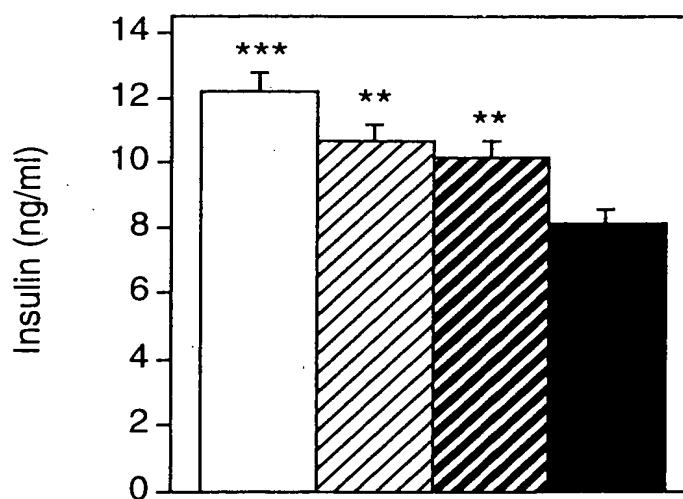
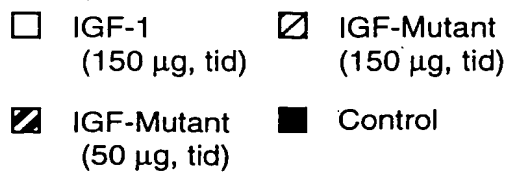


FIG. 23B



plasmid t4.g8
length: 5140 (circular)

1 GAATTCAACT TCTCCATACT TTGATAAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGTCGT TACTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTCTCT TCTCAGCTTA

101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GAGGTACGA AGCGTTATAC CGCGTTTAC TGGTTGTGCG CAACTAAC TA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCAGTA
CCCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTTCACAA GCTGTCATAA AGTTGTCACG GCCGAGACTT ATAGTCGCTT TGTTTTATT TTTTAATGTA TTTGTAACTA GTACGCAAGT
TTTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATCGGTTCA

401 TCACGTAAAA AGGGTATCTA GAGGTTGAGG TGATTTTATG AAAAAGATA TCGCATTTCT TCTTGCACT ATGTTGCTTT TTTCTATTGC TACAAATGCC
AGTGCATTTT TCCCATAGAT CTCCAACCTC ACTAAAATAC TTTTCTCTAT AGCGTAAAGA AGAACGTAGA TACAAGCAAA AAAGATAACG ATGTTTACGG

501 TATGCATCTG GTACCGCCAT GGCTGATCCG AACCGTTTCC GCGGTAAAGA TCTGGCAGGT TCACCAGGTG GAGGATCCGG AGGAGCGCC GAGGGTGACG
ATACGTAGAC CATGGCGGTA CCGACTAGGC TTGGCAAAGG CGCCATTTCT AGACCGTCCA AGTGGTCCAC CTCCTAGGCC TCCTCCGCG CTCGCCACTGC

1 SerG lyThrAlaMe tAlaAspPro AsnArgPheA rgGlyLysAs pleuAlaGly SerProGlyG lyGlySerG lYglyGlyAla GluGlyAspAsp

33 ProAlaLy salaAlaPhe AsnSerLeug lnaLaSerAl aThrGluTyr ileGlyTyrA laTrpAlaMe tValValVal ileValGlyA laThrIleGly

601 ATCCCGCAAA AGCGGCCTTT AACTCCCTGC AAGCCTCAGC GACCGAATAT ATCGGTTATG CGTGGGCGAT GGTGTTGTGTC ATTGTCGGCG CAACATATCGG
TAGGGCGTTT TCGCCGGAAA TTGAGGGACG TTCGGAGTCG CTGGCTTATA TAGCCAATAC GCACCCGCTA CCAACAACAG TAACAGCCGC GTTGATAGCC

701 TATCAAGCTG TTTAAGAAAT TCACCTCGAA AGCAAGCTGA TAAACCGATA CAATTAAAGG CTCCTTTTGG AGCCTTTTTT TTTGGAGATT TTCAACGTGA
ATAGTTCGAC AAATTCTTTA AGTGGAGCTT TCGTTCGACT ATTTGGCTAT GTTAATTTC GAGGAAAAACC TCGGAAAAAA AAACCTCTAA AAGTTGCACT

66 ileLysLeu PheLysLysP heThrSerLy salaSer

801 AAAAATTATT ATTGCAATT CCTTTAGTTG TTCTCACTCC GCTGAAACTG TTGAAAGTTG TTAGCAAAA CCCCATACAG AAAATTCAAT
TTTTTAATAA TAAGCGTTAA GGAATCAAC AAGGAAAGAT AAGAGTGAGG CGACTTGAC AACTTTCAAC AAATCGTTTT GGGGTATGTC TTTTAAGTAA

901 TACTAACGTC TGGAAAGACG ACAAACCTT AGATCGTTAC GCTAACTATG AGGTTGTCT GTGGAATGCT ACAGCGTTG TAGTTGTAC TGGTGACGAA
ATGATTGCAG ACCTTTCTGC TGTTTTGAAA TCTAGCAATG CGATTGATAC TCCCAACAGA CACCTTACGA TGTCGCAAC ATCAAAACATG ACCACTGCTT

1001 ACTCAGTGC TAGCTAGAGT GGGGTGGCT CTGGTTCCGG TGATTTTGAT TATGAAAAGA TGGCAACCG TAATAAGGG GCTATGACCG AAAATGCCGA
TGAGTCACAG ATCGATCTCA CCGCCACCGA GACCAAGGCC ACTAAAATA ATACTTTCT ACCGTTTGGG ATTTATTTCCC CGATACTGGC TTTTACGGCT

FIG. 24A





1101 TGAAAAACGG CTACAGTCTG ACGCTAAAGG CAAAACCTTGAT TCTGTCGCTA CTGATTACGG TGCTGCTATC GATGGTTTCA TTGGTGACGT TTCCGGCCTT
ACTTTTGGCG GATGTCAGAC TGGGATTTC GTTTGAACCTA AGACAGCGAT GACTAATGCC ACGACGATAG CTACCAAGT AACCACTGCA AAGCCGGGAA

1201 GCTAATGGTA ATGGTGCTAC TGGTGATTTT GCTGGCTCTA ATTCCCAAT GGCTCAAGTC GGTGACGGTG ATAAATCACC TTAAATGAAT AATTCCGTC
CGATTACCAT TACCACGATG ACCACTAAAA CGACCGAGAT TAAGGGTTTA CCGAGTTTCA CCACTGCCAC TATTAAGTGG AAATTACTTA TTAAAGGCAG

1301 AATATTATCC TTCCCTCCCT CAATCGGTTG AATGTCGCCC TTTTGTCTTT AGCGTGGTA AACCATATGA ATTTCTTATT GATTGTGACA AAATAAACTT
TTATAAATGG AAGGGAGGA GTTAGCCAC GTTAGCCAC AAAACAGAAA TCGCGACCAT TTGGTATACT TAAAAAGATAA CTAACACTGT TTTATTGAA

1401 ATTCCGTGGT GTCTTTGCGT TTCTTTTATA TGTGGCCACC TTTATGATG TATTTTCTAC GTTTGCTAAC ATACTGCGTA ATAAGGAGTC TTAATCATGC
TAAGGCACCA CAGAAACGCA AAGAAATAT ACAACGGTGG AAATACATAC ATAAAAGATG CAAACGATTG TATGACGCAT TATTCCTCAG AATTAGTACG

3201 ACTCAAAGGC GGTAAATACGG TTATCCACAG AATCAGGGGA TAACGCAGGA AAGAACATGT GAGCAAAAGG CCAGCAAAAG GCCAGGAACC GTAAAAAGGC
TGAGTTTCCG CCATTATGCC AATAGGTGTC TTAGTCCCTT ATTGCGTCCCT TTCTTGATACA CTCGTTTTCC GGTGCTTTGG CATTTTCCG

3301 CGCGTTGCTG GCGTTTTC ATAGGCTCCG CCCCCCTGAC GAGCATCACA AAAATCGACG CTCAAAGTCAG AGGTGGCGAA ACCCGACAGG ACTATAAAGA
GCGCAACGAC CGCAAAAAGG TATCCGAGGC GGGGGGACTG CTCGTAGTGT TTTTAGCTGC GAGTTCAGTC TCCACCGCTT TGGGCTGTCC TGATATTCT

3401 TACCAGGCGT TTCCCTCTGG AAGCTCCCTC GTGGCTCTC CTGTTCCGAC CCGTCCGCTT ACCGGATACC TGTCGCGCTT TCTCCCTTCG GGAAGCGTGG
ATGTTCCGCA AAGGGGACC TTGAGGGAG CACGCGAGAG GACAAGGCTG GAGCGGCGAA TGGCCTATGG ACAGGCGGAA AGAGGGAAGC CCTTCGCACC

3501 CGCTTTCTCA TAGTCACGC TGTAGGTATC TCAGTTCCGT GTAGGTCGTT CGCTCCAAGC TGGGCTGTGT GCAGCAACCC CCGTTTCAGC CCGACCGCTG
GGGAAAGAT ATCAGTGCG ACATCCATAG AGTCAAGCCA CATCCAGCAA GCGAGGTTTC ACCCGACACA CGTGTGTTGG GGGCAAGTCG GGCTGGCGAC

3601 CGCCTTATCC GGTAACTATC GTCTTGAGTC CAACCCGGTA AGACACGACT TATGCCCACT GGCAGCAGCC ACTGGTAACA GGATTAGCAG AGCGAGGTAT
GGGAATAGG CCATTGATAG CAGAACTCAG GTTGGGCCAT TCTGTGCTGA ATAGCGGTGA CCGTCGTCGG TGACCATGT CCTAATCGTC TCGTCCATA

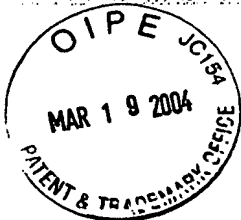
3701 GTAGGCGGTG CTACAGAGTT CTTGAAGTGG TGGCTTAAC TGGCTACAC TAGAAGGACA GTATTTGGTA TCTGCGCTCT GCTGAAGCCA GTTACCTTCG
CATCCGCCAC GATGCTCAA GAACCTCAC ACCGGATTGA TGCCGATGT ATCTTCTGT CATAAACCAT AGACGCGAGA CGACTTCGT CATGGAAGC

3801 GAAAAAGAT TGGTAGTCT TGATCCGGCA AACAAACCAAC CGCTGGTAGC GGTGGTTTTT TTGTTTGCAA GCAGCAGATT ACGCGCAGAA AAAAAGGATC
CTTTTCTCA ACCATCGAGA ACTAGGCCGT TTGTTGGTG GCGACCATCG CCACCAAAAA AACAAACGTT CGTCGCTTAA TGCGGCTCTT TTTTCCCTAG

3901 TCAAGAAGAT CCTTTGATCT TTTCTACGG GTCTGACGCT CAGTGGAAACG AAAACTCAGG TTAAGGGATT TTGGTCATGA GATTATCAA AAGGATCTTC
AGTCTTCTA GGAACCTAGA AAAGATGCC CAGACTGCGA GTCACTTGC TTTTGAGTGC AATTCCCTAA AACCACTACT CTAATAGTTT TTCCTAGAAG

4001 ACCTAGATCC TTTTAAATTA AAAATGAAGT TTTAAATCAA TCTAAAGTAT ATATGAGTAA ACTTGGTCTG ACAGTTACCA ATGCTTAATC AGTGAGGCAC
TGGATCTAGG AAAATTAAAT TTTTACTTCA AAATTAGTT AGATTTCTA TATACTCAT TGAACAGAC TGTCAATGGT TACGAATTAG TCACTCCGTG

FIG. 24B



4101 CTATCTCAGC GATCTGTCTA TTTCTGTTTCAT CCATAGTTGC CTGACTCCCC GTCGTGTAGA TAACATAGAT ACGGAGGGC TTACCATCTG GCCCCAGTGC
GATAGAGTCG CTAGACAGAT AAGCAAGTA GGTATCAACG GACTGAGGG GAGCATCT ATTGATGCTA TGCCCTCCCG AATGGTAGAC CGGGGTACG

4201 TGCAATGATA CCGCGAGACC CACGCTCACC GGCTCCAGAT TTATCAGCAA TAAACCAGCC AGCCGGAAGG GCCGAGCGCA GAAGTGGTCC TGCAACTTTA
ACGTTACTAT GCGCTCTGG GTGCGAGTGG CCGAGGTCTA AATAGTCTT ATTGGTCCG TCGGCTTCC CGGCTCGCGT CTTACCCAGG ACGTTGAAAT

4301 TCCGCCCTCA TCCAGTCTAT TAAATTGTTGC CCGGAAGCTA GAGTAAGTAG TTGCCCAGTT AATAGTTTGC GCAACGTTGT TGCCATTGCT GCAGGCATCG
AGGCGGAGGT AGGTCAGATA ATTAACACAG GCCCTTCGAT CTCAATTCATC AAGCGGTCAA TTATCAAAAG CGTTGCAACA ACGGTAACGA CGTCCGTAGC

4401 TGGTGTACG CTCGTGTTT GGTATGGCTT CATTGAGCTC CGGTTCCCAA CGATCAAGGC GAGTTACATG ATCCCCCATG TTGTGCAAAA AAGCGGTTAG
ACCAACAGTC GAGCAGCAAA CCATACCGAA GTAAGTCGAG GCCAAGGTT GCTAGTTCCG CTCAATGTAC TAGGGGGTAC AACACGTTTT TTCGCCAATC

4501 CTCCTTCGGT CCTCCGATCG TTGTCAGAAG TAAAGTTGGCC GCAGTGTAT CACTCATGGT TATGGCAGCA CTGCATAATT CTCTTACTGT CATGCCATCC
GAGGAAGCCA GGAGGCTAGC AACAGTCTT ATTCAACCGG CGTCACAATA GTGAGTACCA ATACCGTCTG GACGTATTAA GAGAATGACA GTACGGTAGG

4601 GTAAGATGCT TTTCTGTGAC TGGTGAGTAC TCAACCAAGT CATTCTGAGA ATAGTGTATG CCGCGACCGA GTTGCTCTTG CCCGGCGTCA ACACGGGATA
CATTCTACGA AAGACACTG ACCACTCATG AGTTGGTTCA GTAAGACTCT TATCACATAC GCCGCTGGCT CAACGAGAAC GGGCCGCAGT TGTGCCCTAT

4701 ATACCGCGCC ACATAGCAGA ACTTTAAAAG TGCTCATCAT TGGAAAACGT TCTTCGGGGC GAAAACCTCTC AAGGATCTTA CCGCTGTTGA GATCCAGTTC
TATGGCGCGG TGTATCGTCT TGAAATTTT ACAGTAGTA ACCTTTTGCA AGAAGCCCCG CTTTTGAGAG TTCCCTAGAAAT GCGGACAACT CTAGGTCAAG

4801 GATGTAACCC ACTCGTGCAC CCAACTGATC TTCAGCATCT TTTACTTTCA CCAGCGTTTC TGGGTGAGCA AAAACAGGAA GGCAAAATGC CGCAAAAAAG
CTACATTGGG TGAGCACGTG GGTGACTAG AAGTCGTAGA AAATGAAAAG GGTGCAAAAG ACCCACTCGT TTTTGTCTCTT CCGTTTTTACG GCGTTTTTTC

4901 GGAATAAGG CGACACGGA ATGTTGAATA CTCATACTCT TCCCTTTTCA ATATTATTGA AGCATTTATC AGGGTTATTG TCTCATGAGC GGATACATAT
CCTTATTTCC GCTGTGCCTT TACAACCTAT GAGTATGAGA AGGAAAAAGT TATAATAAAT TCGTAAATAG TCCCAATAAC AGAGTACTCG CCTATGTATA

5001 TTGAATGTAT TTAGAAAAAT AAACAAATAG GGGTTCCGGG CACATTTCCC CGAAAAAGTGC CACCTGACGT CTAAGAAAAC ATTATTATCA TGACATTAAC
AACTTACATA AATCTTTTTA TTTGTTTATC CCCAAGGCG GTGTAAAGGG GCTTTTCAG GTGGACTGCA GATTCCTTTGG TAATAATAGT ACTGTAATTG

5101 CTATAAAAAAT AGGCGTATCA CGAGGCCCTT TCGTCTTCAA
GATATTTTTA TCCGCATAGT GCTCCGGGAA AGCAGAAATT

FIG. 24C

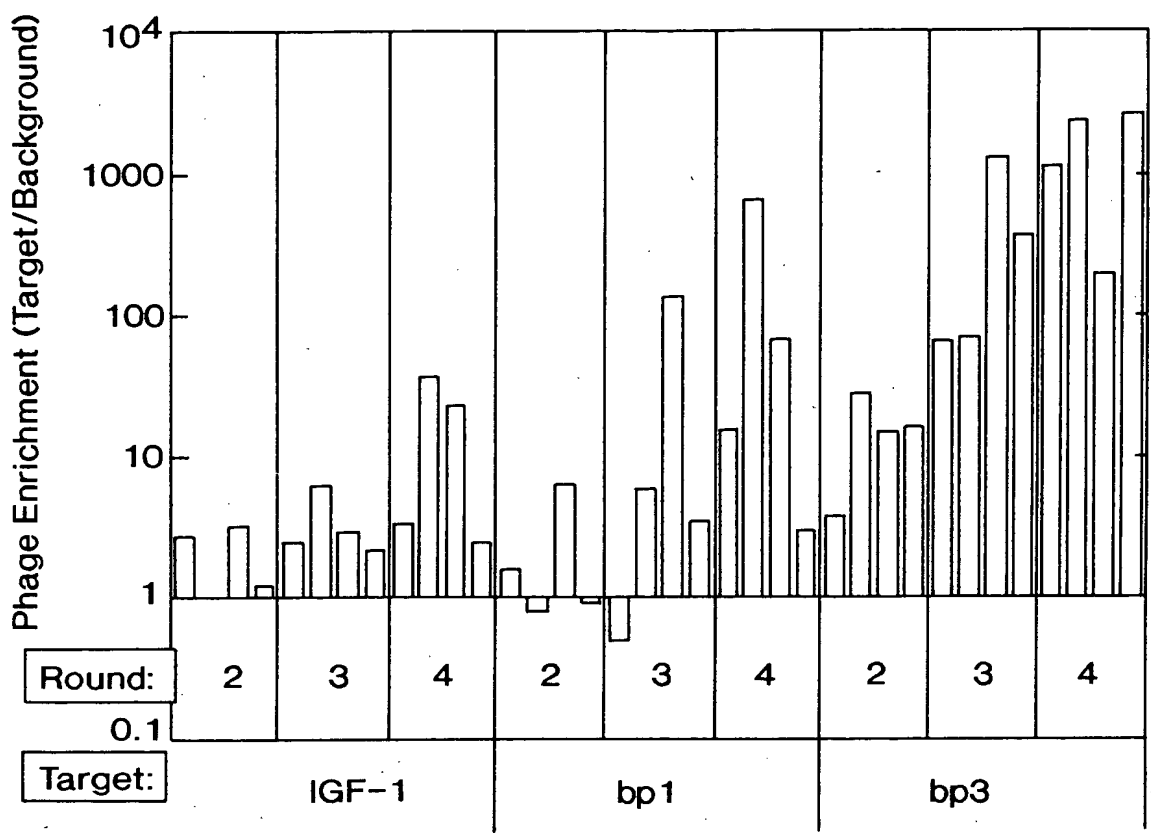


FIG. 25

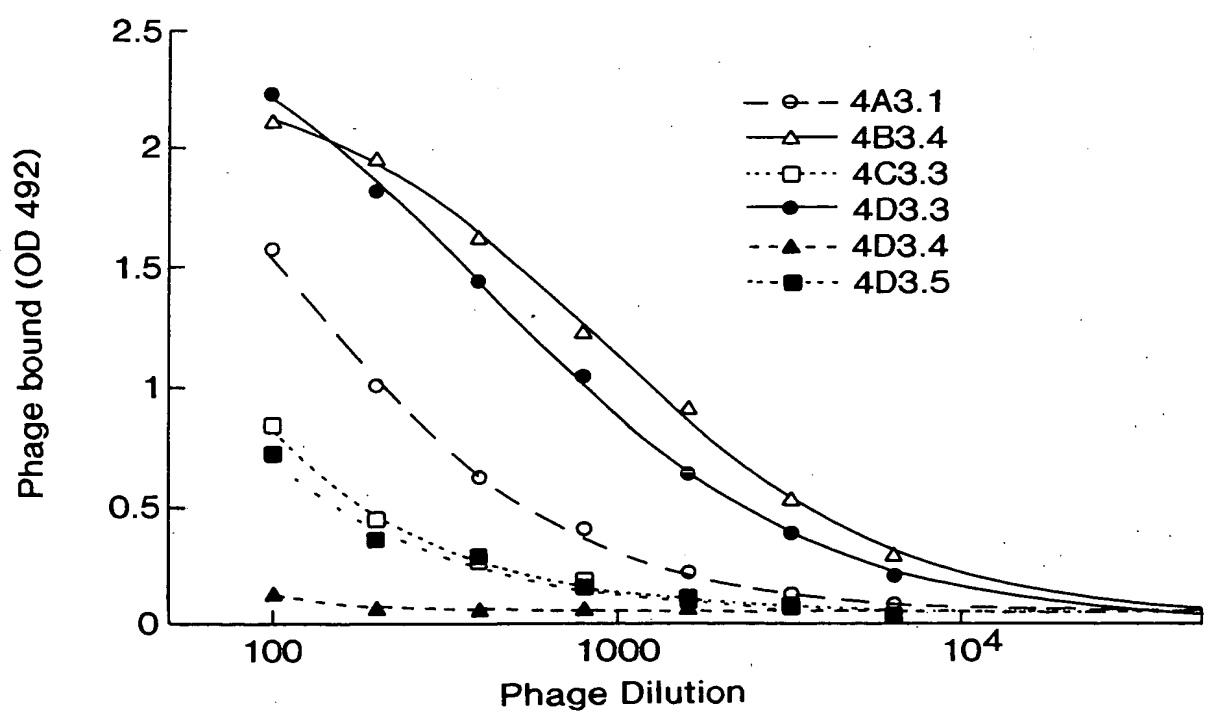


FIG. 26

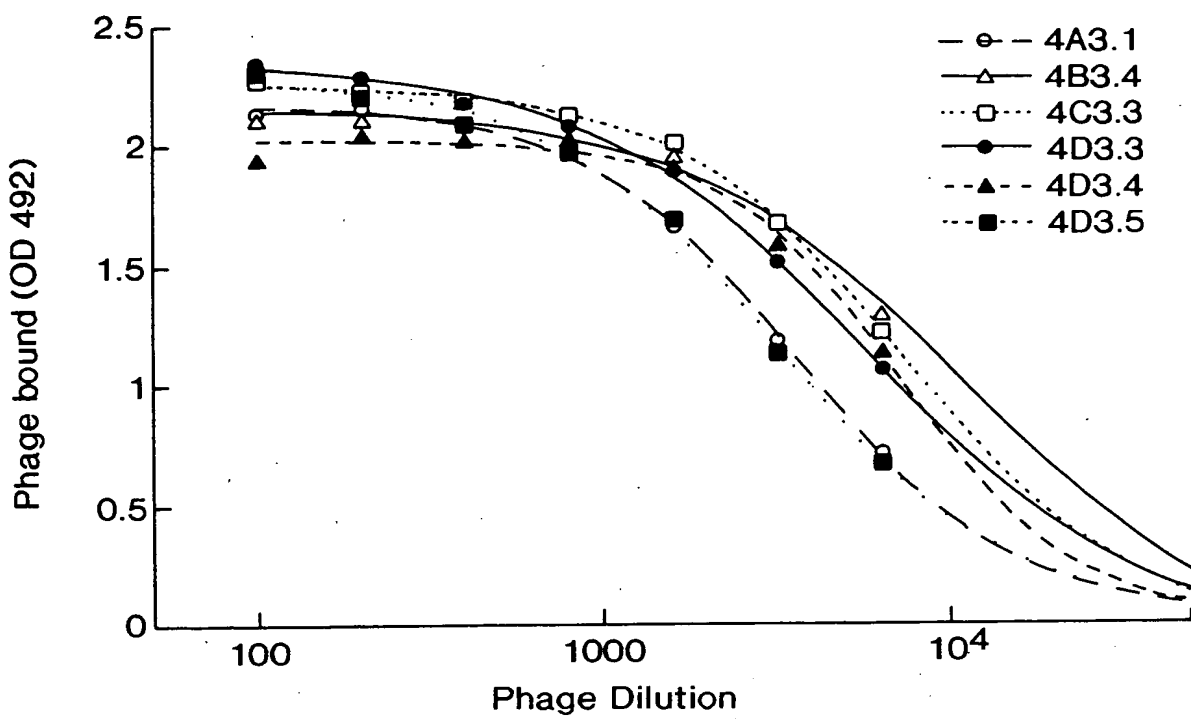


FIG. 27

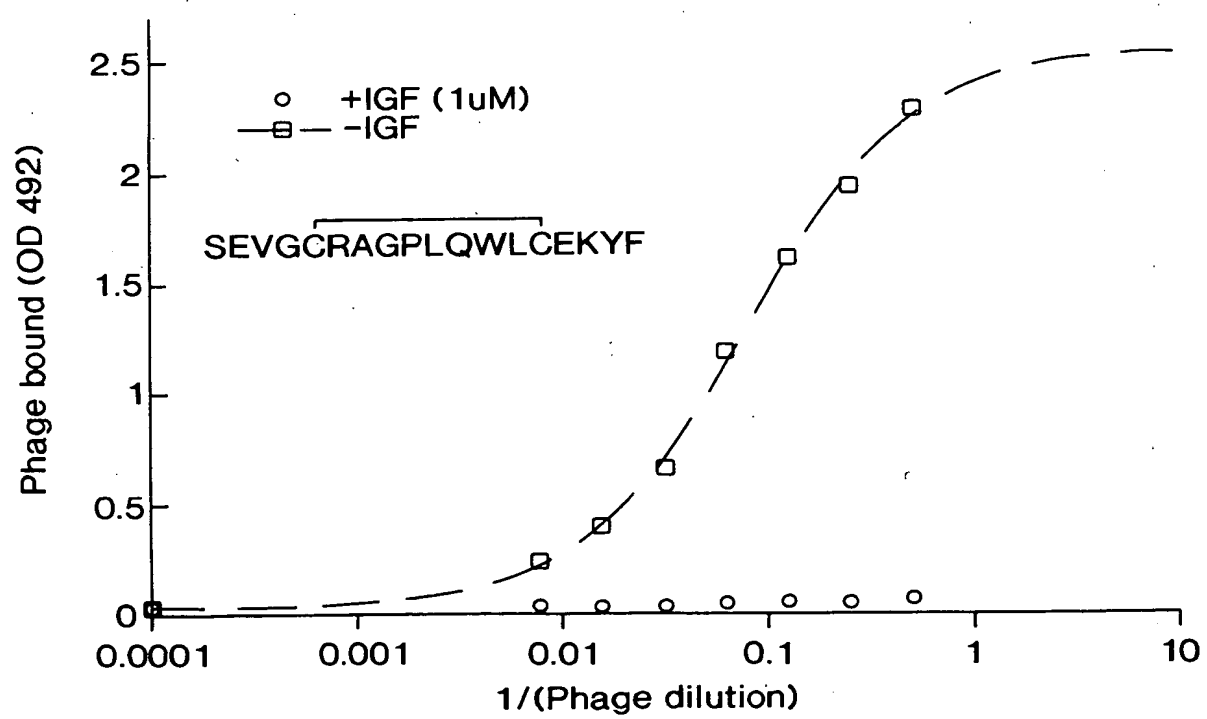


FIG. 28

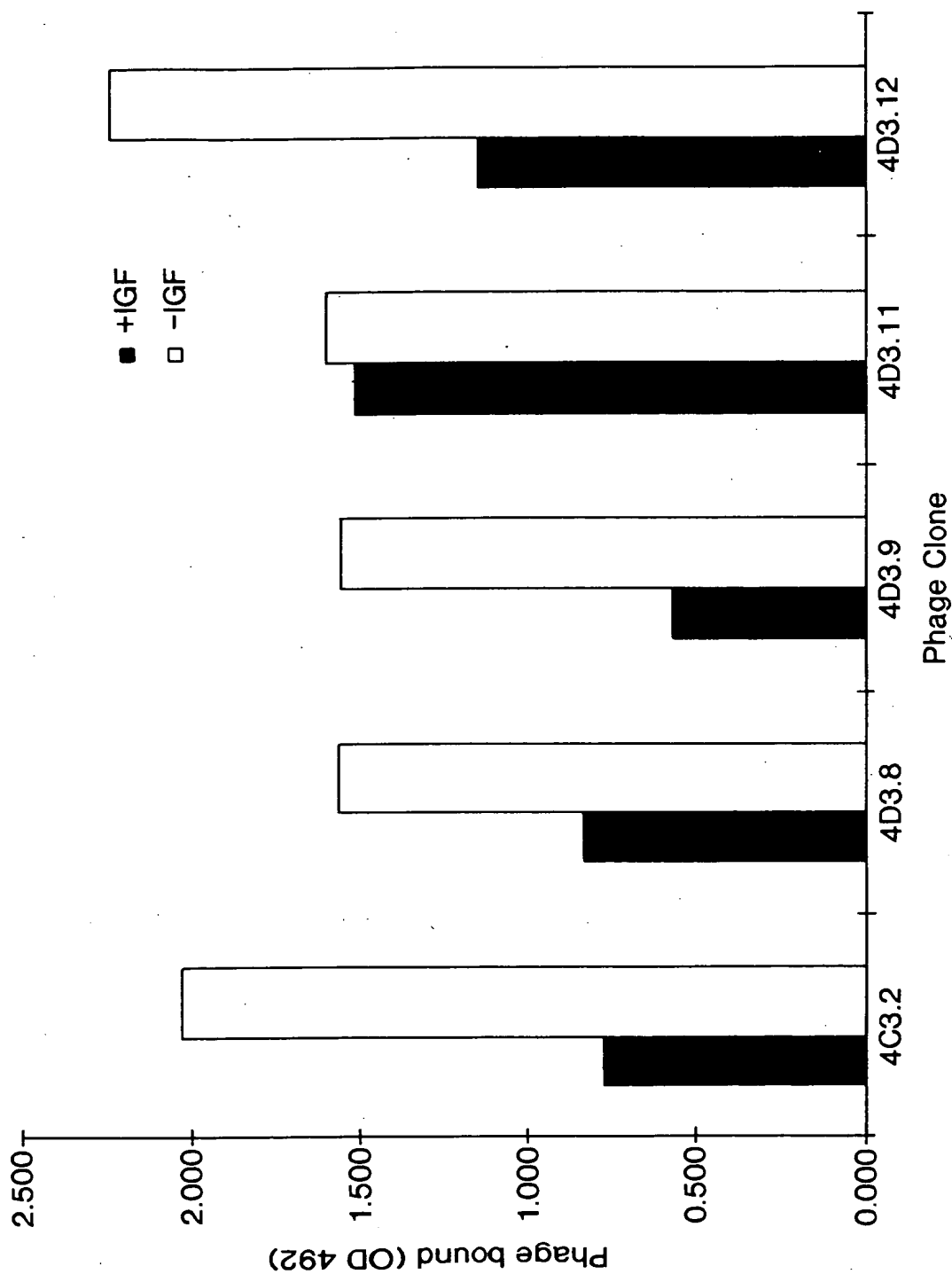


FIG. 29

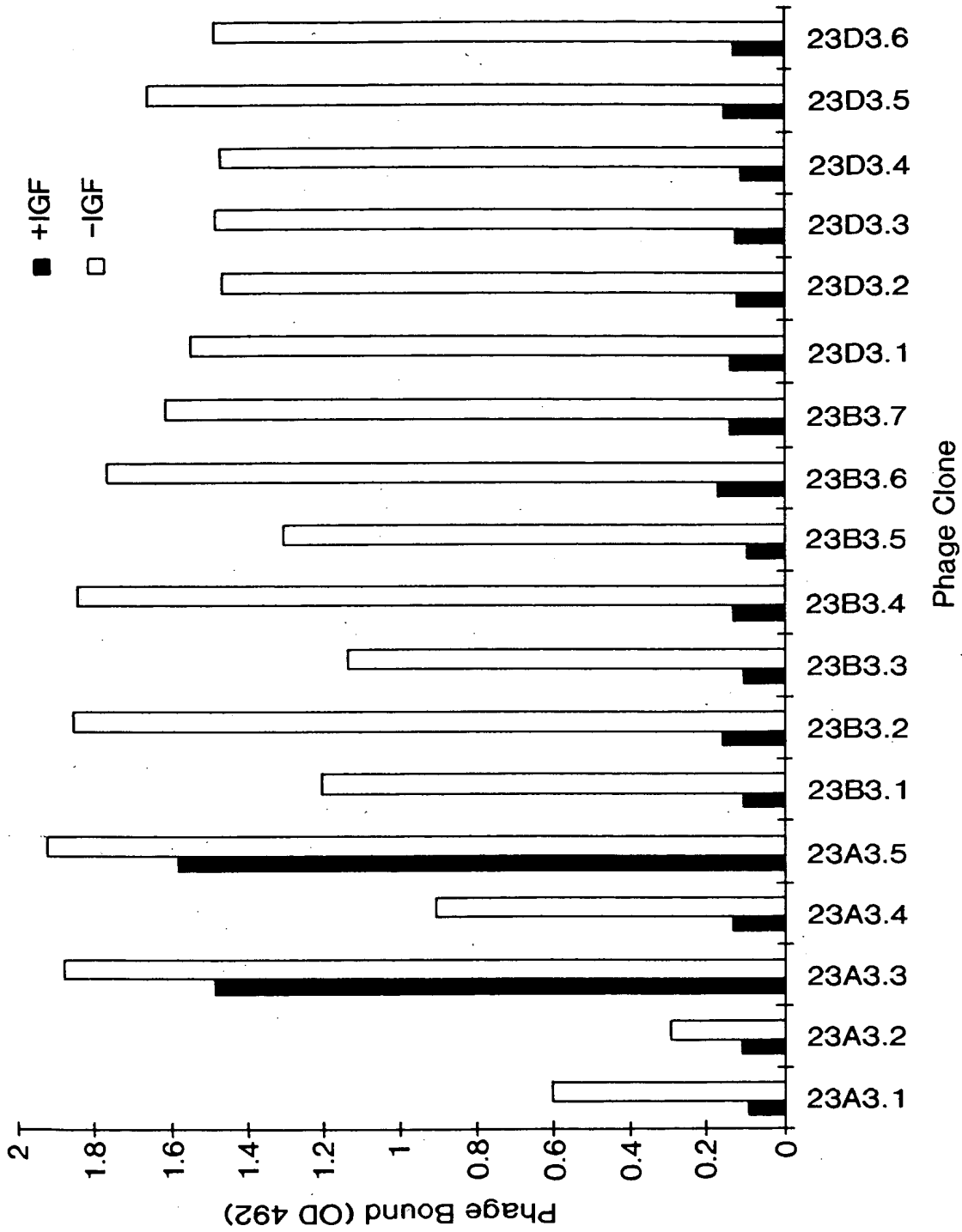


FIG. 30

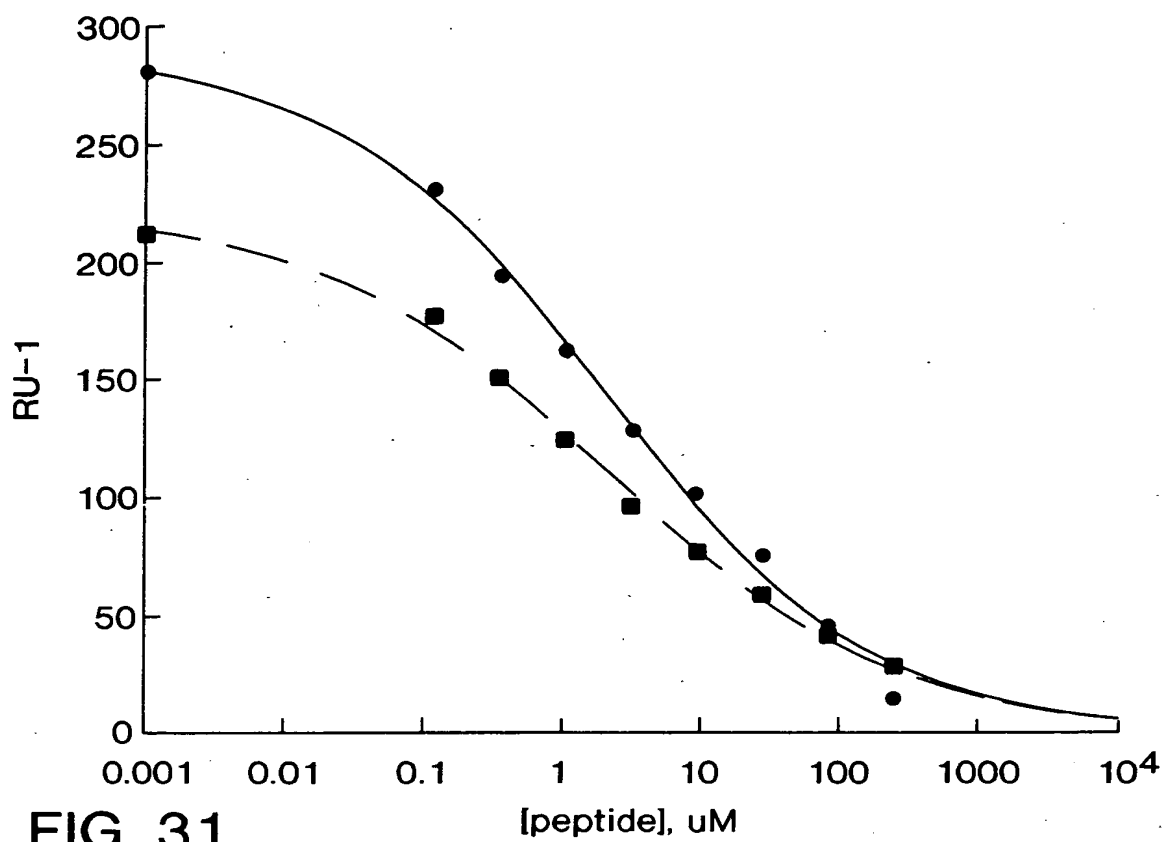


FIG. 31

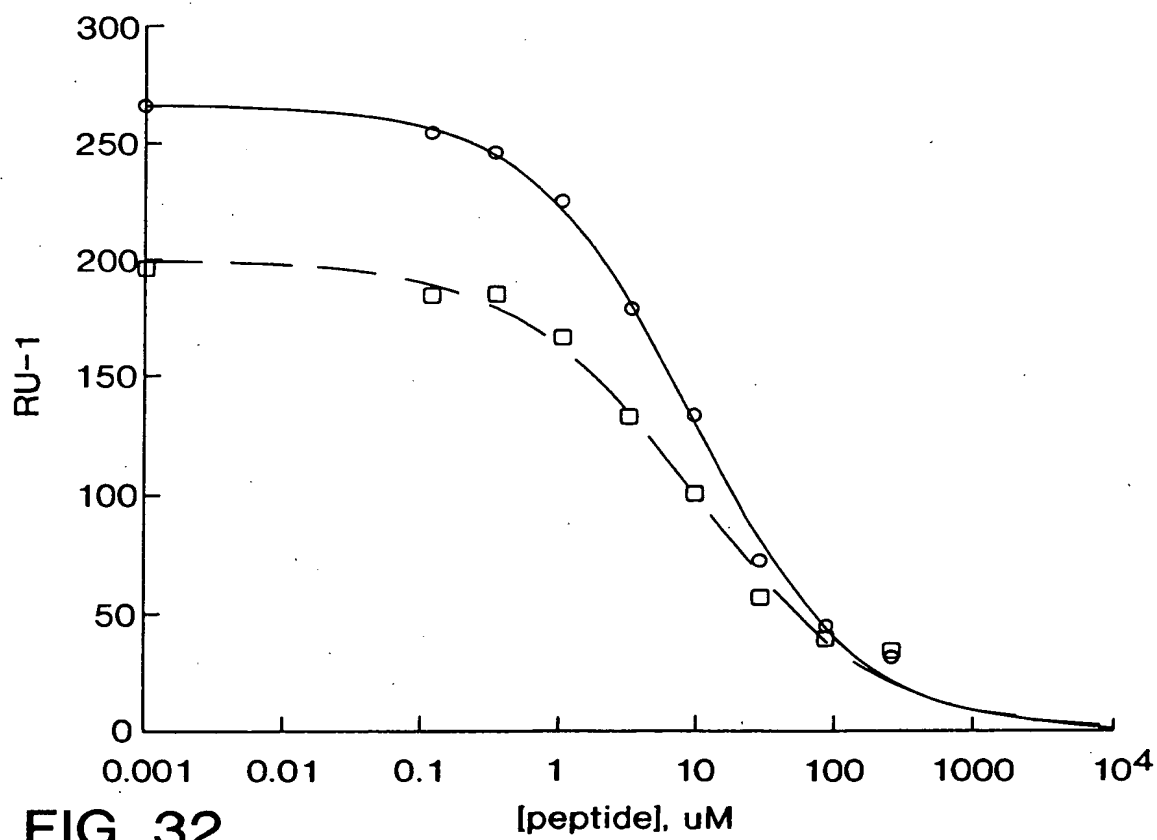


FIG. 32

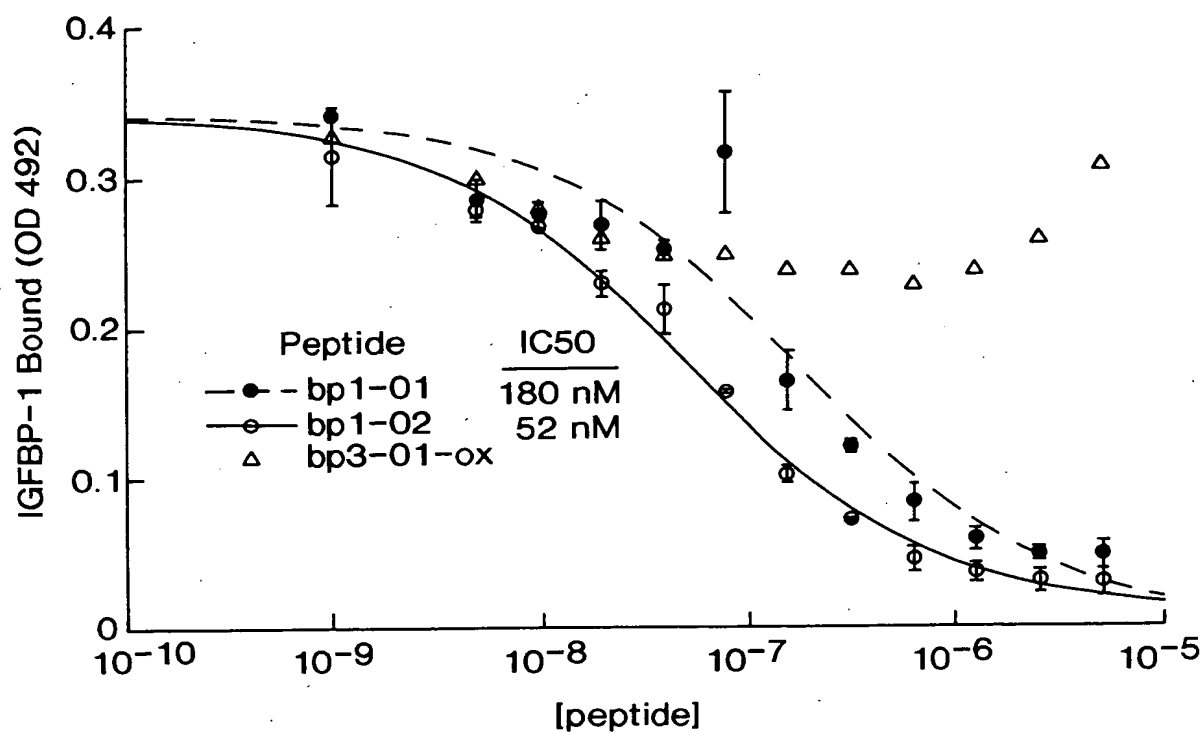


FIG. 33

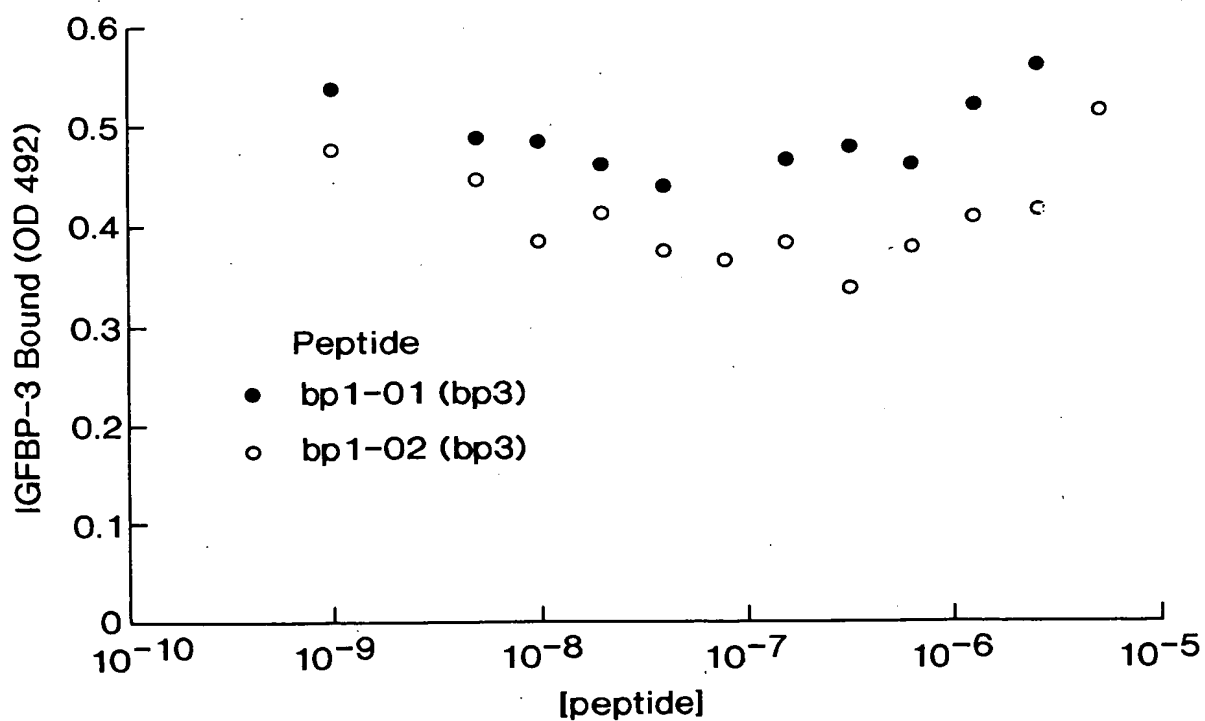


FIG. 34

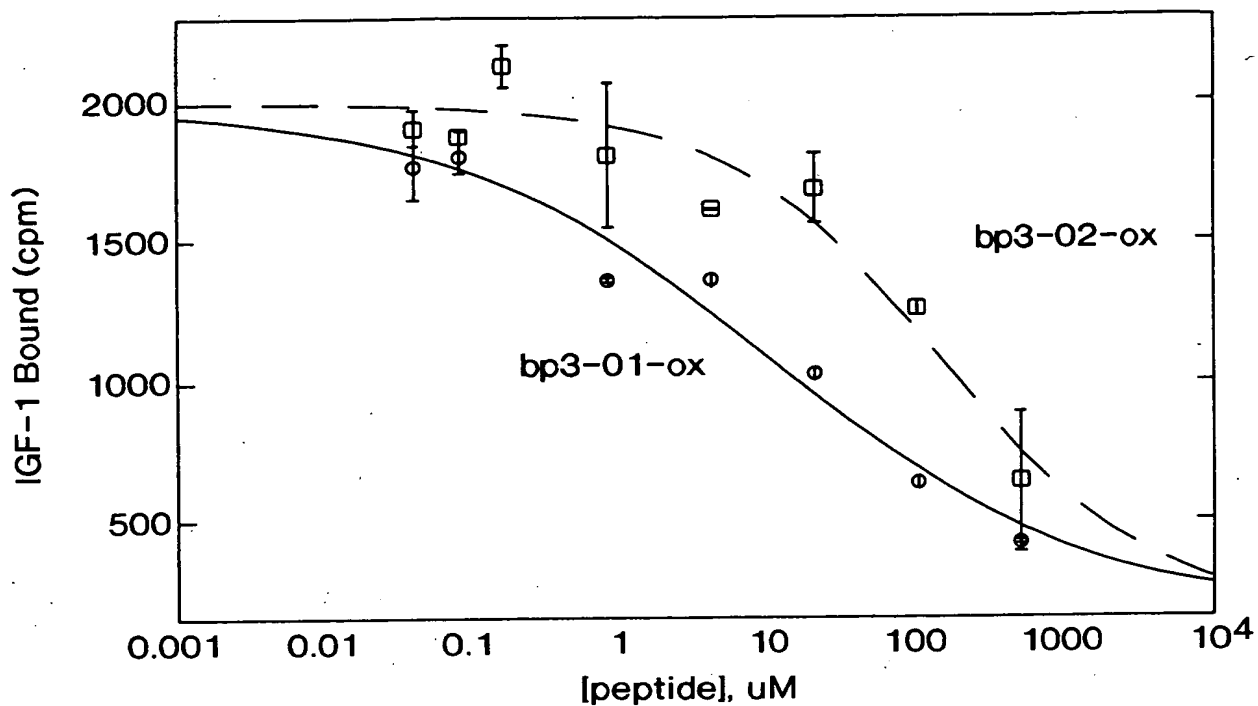


FIG. 35

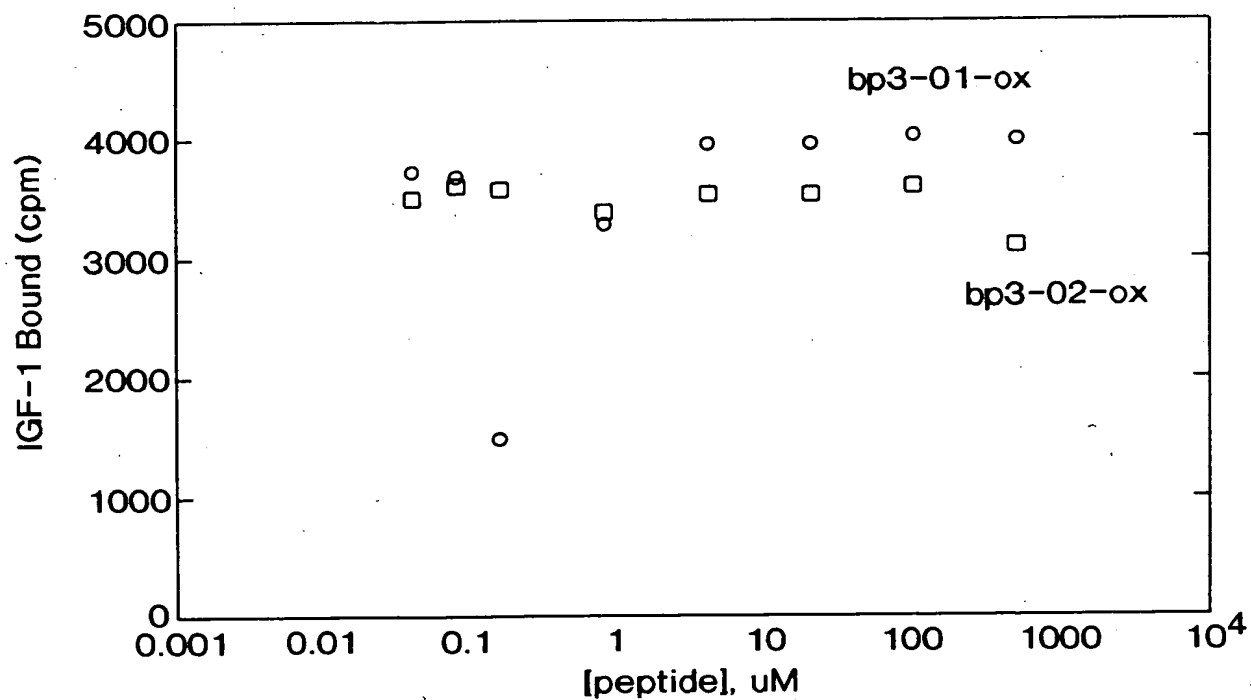


FIG. 36

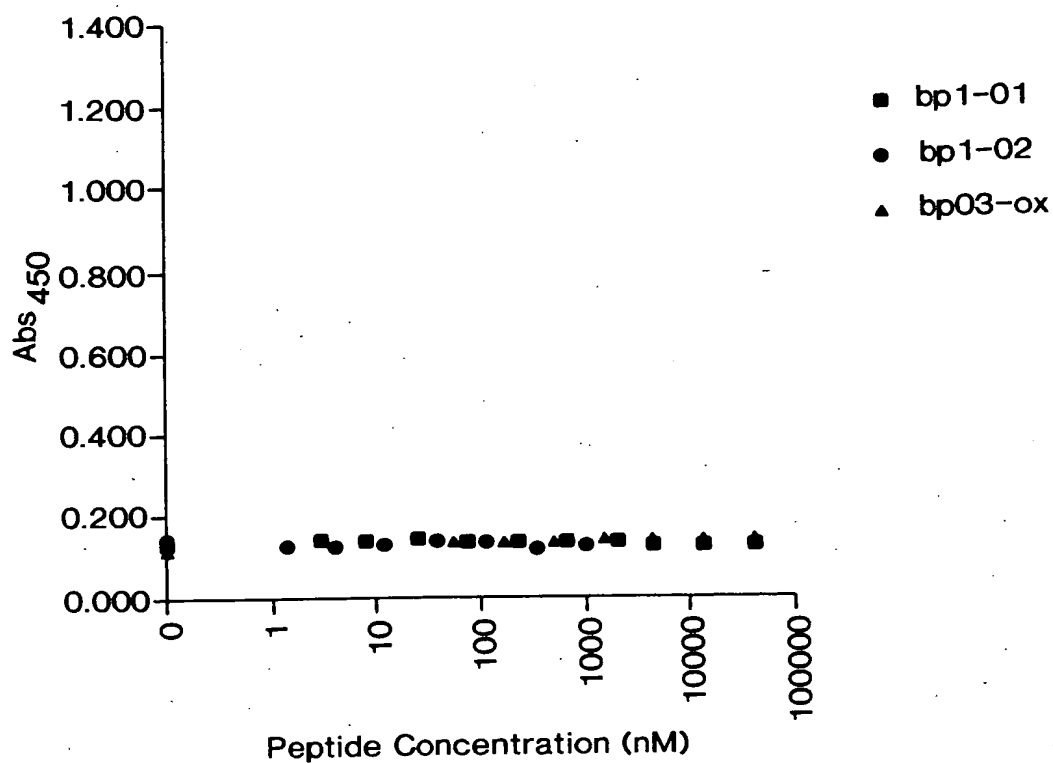
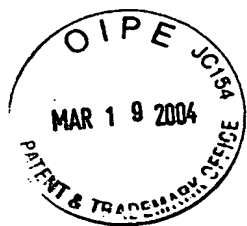


FIG. 37A

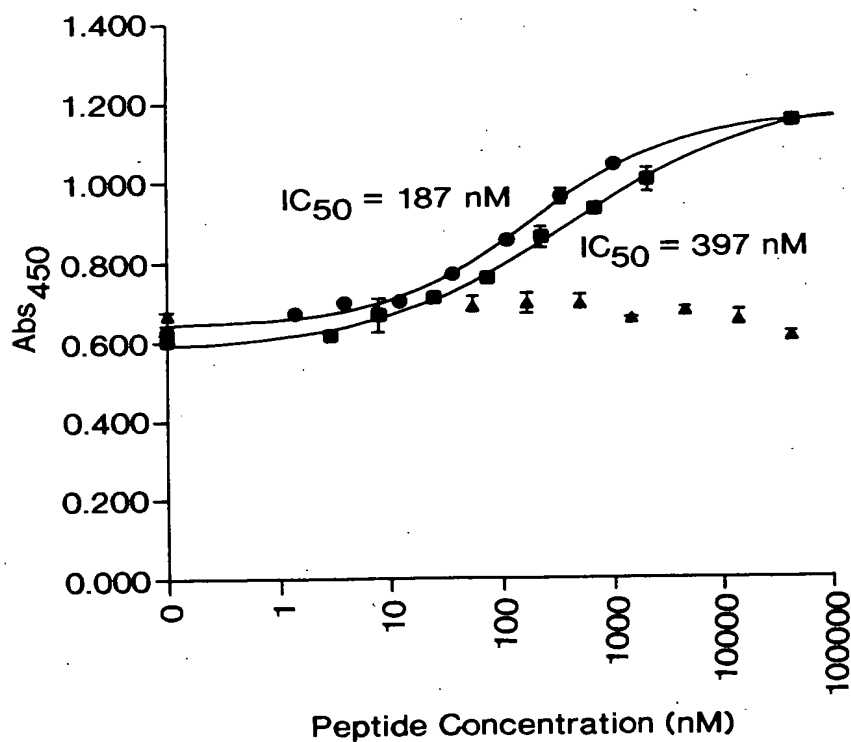


FIG. 37B

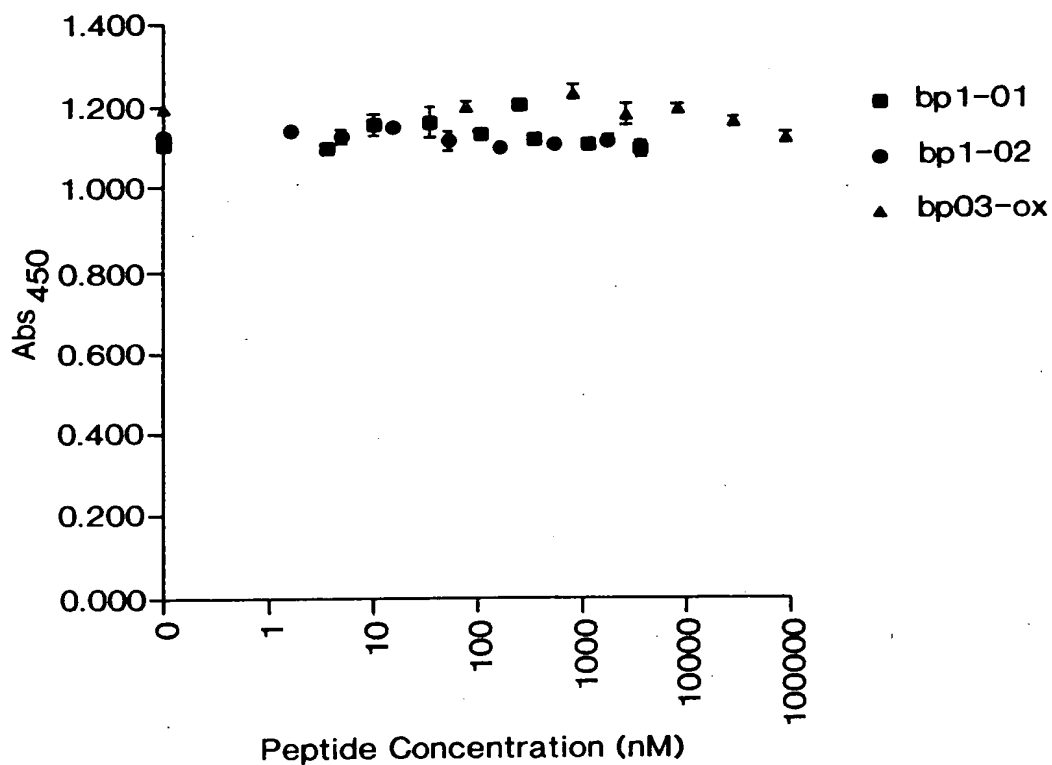


FIG. 37C

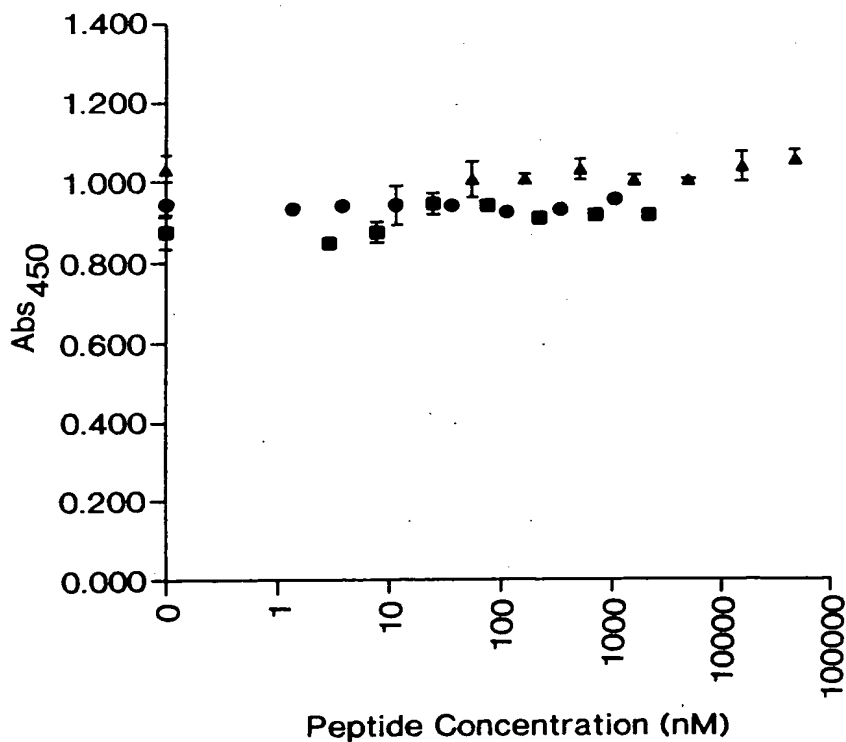


FIG. 37D

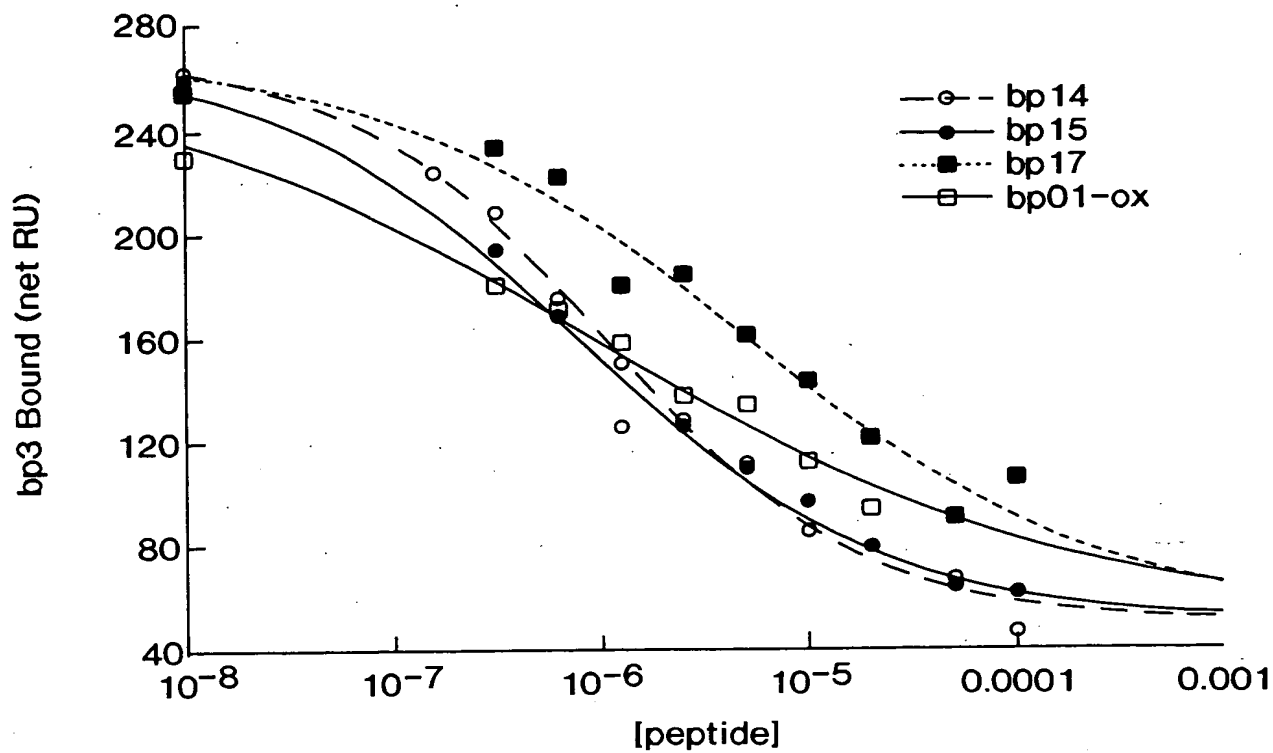


FIG. 38

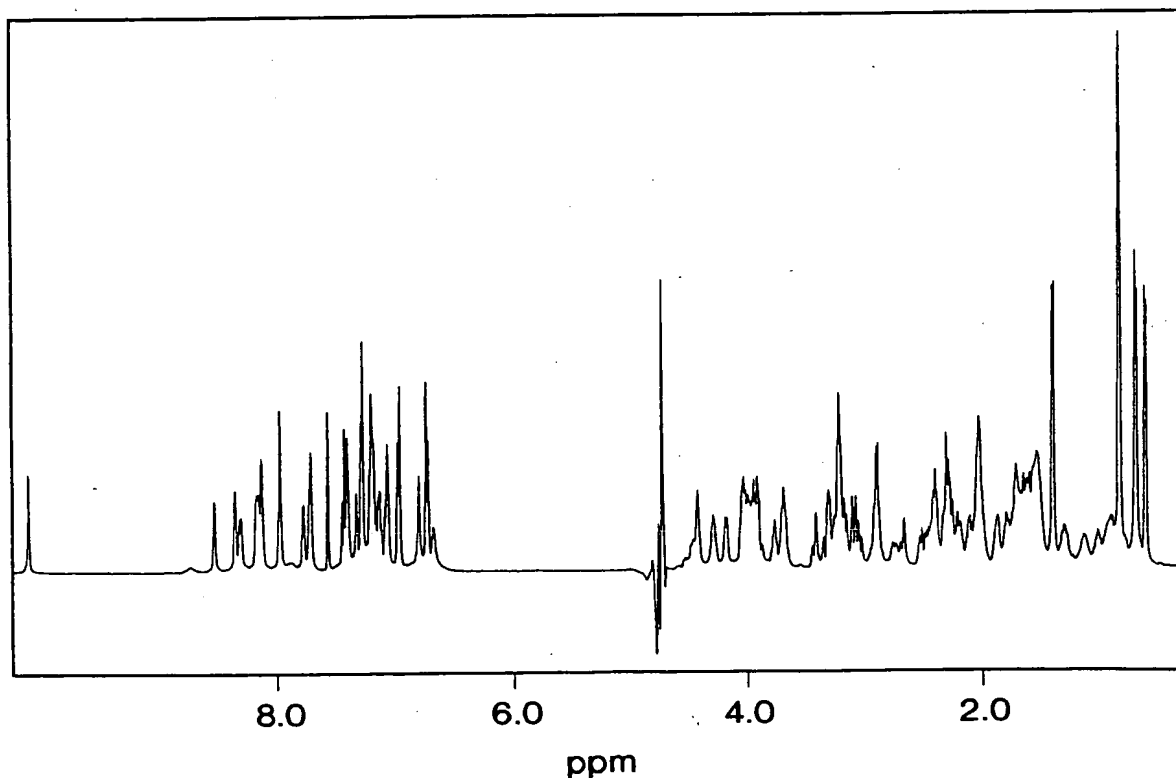


FIG. 39

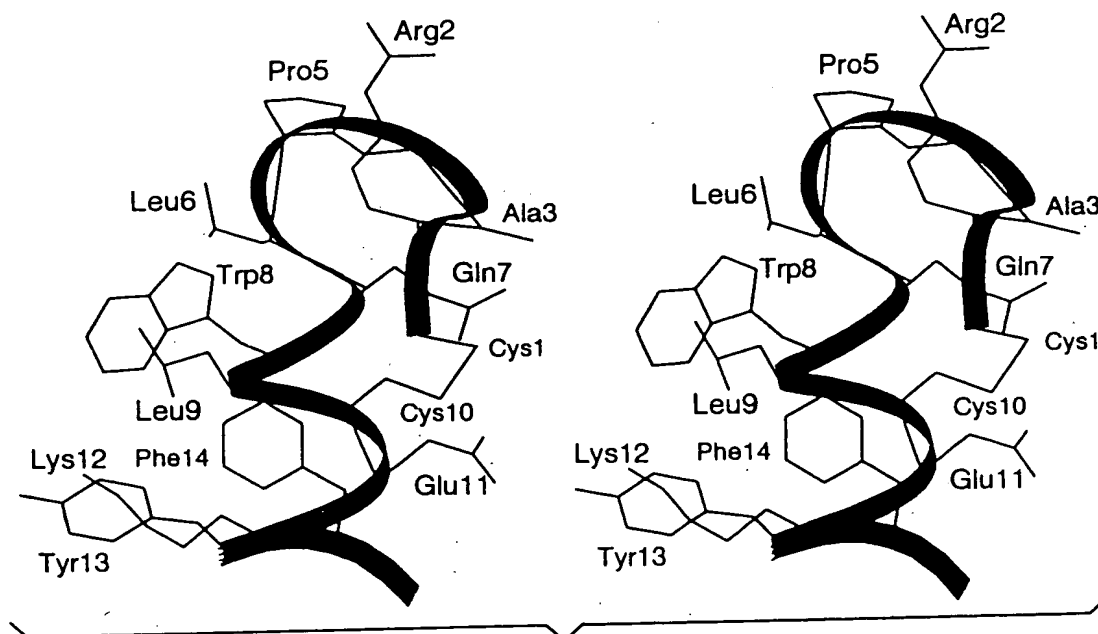


FIG. 40A

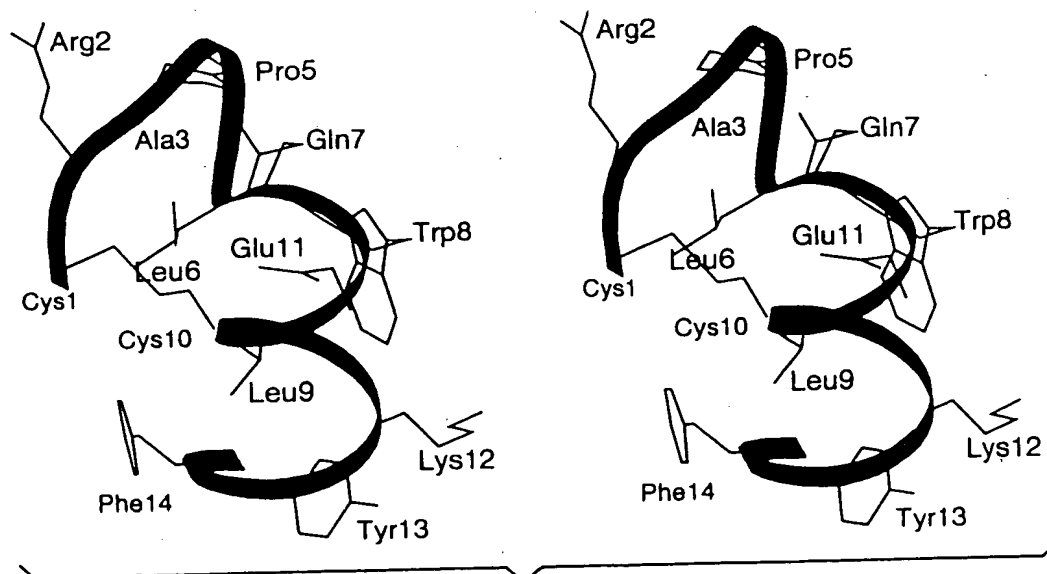


FIG. 40B

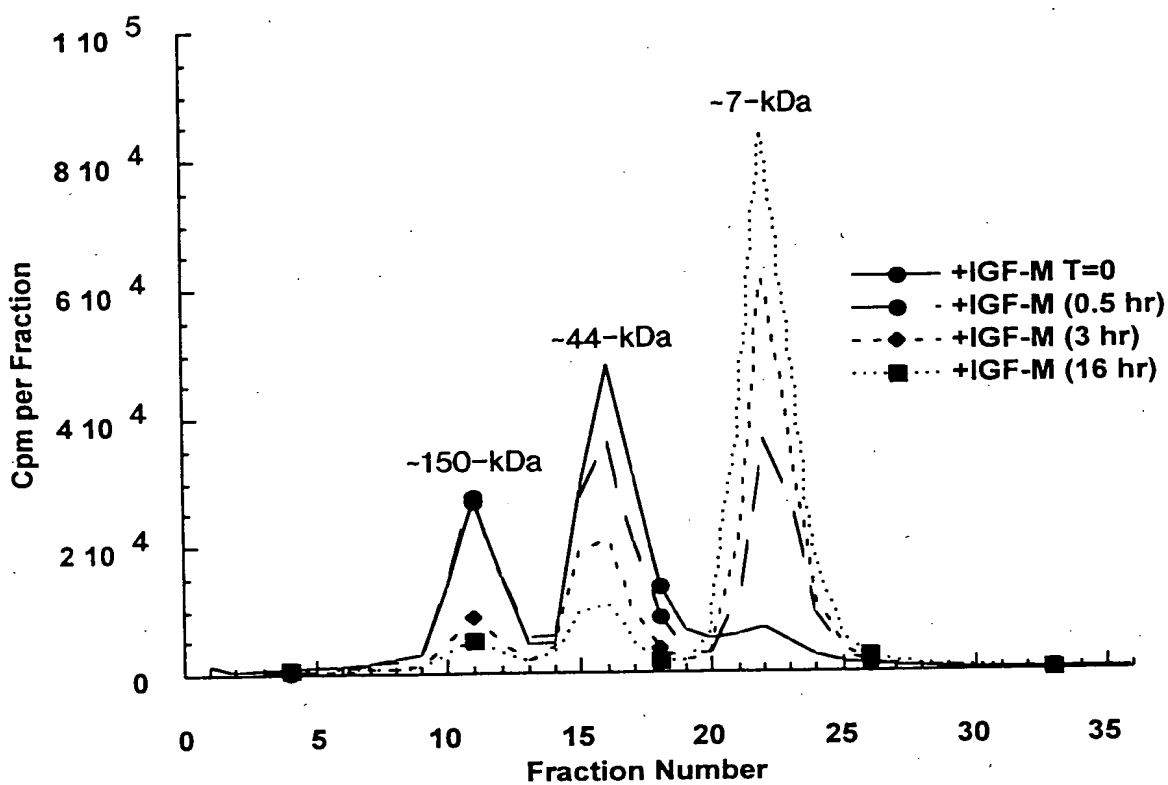
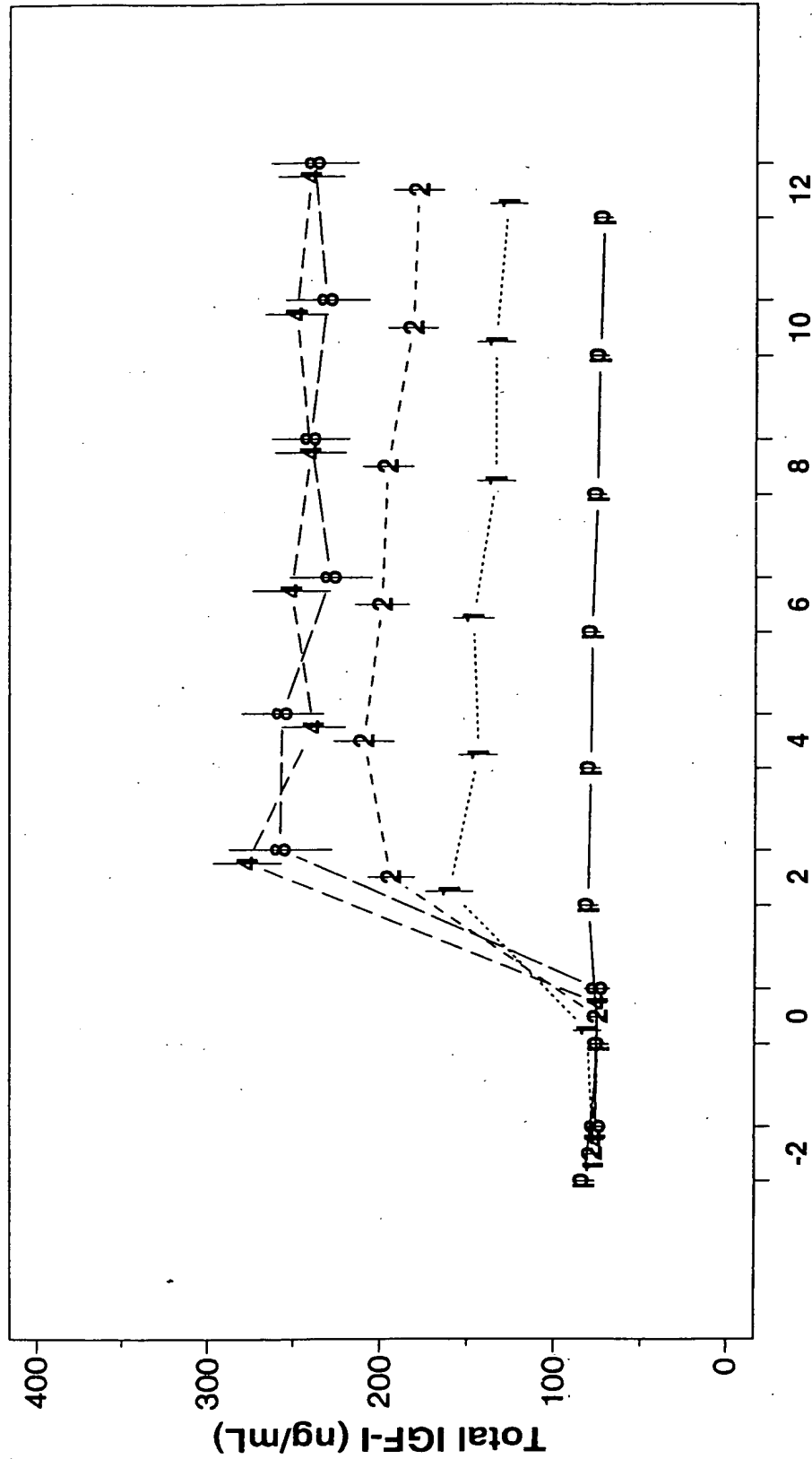


FIG. 41



Effect of IGF-I Treatment on Total IGF-I

(Mean \pm SE)

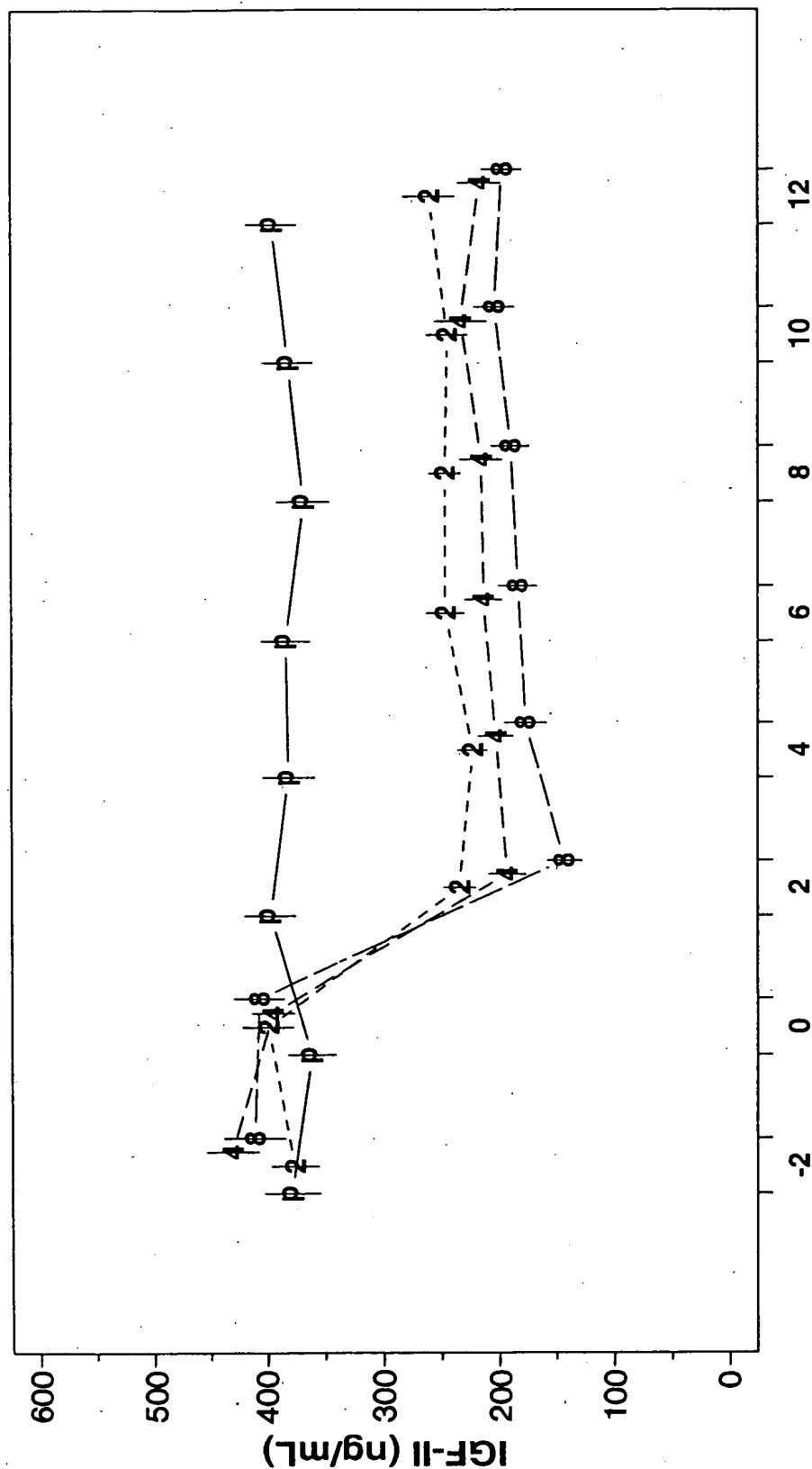


Treatment Visits (Week)

FIG. 42

Effect of IGF-I Treatment on IGF-II

(Mean \pm SE)



Treatment Visits (Week)

FIG. 43



Effect of IGF-I Treatment on IGFBP-3

(Mean \pm SE)

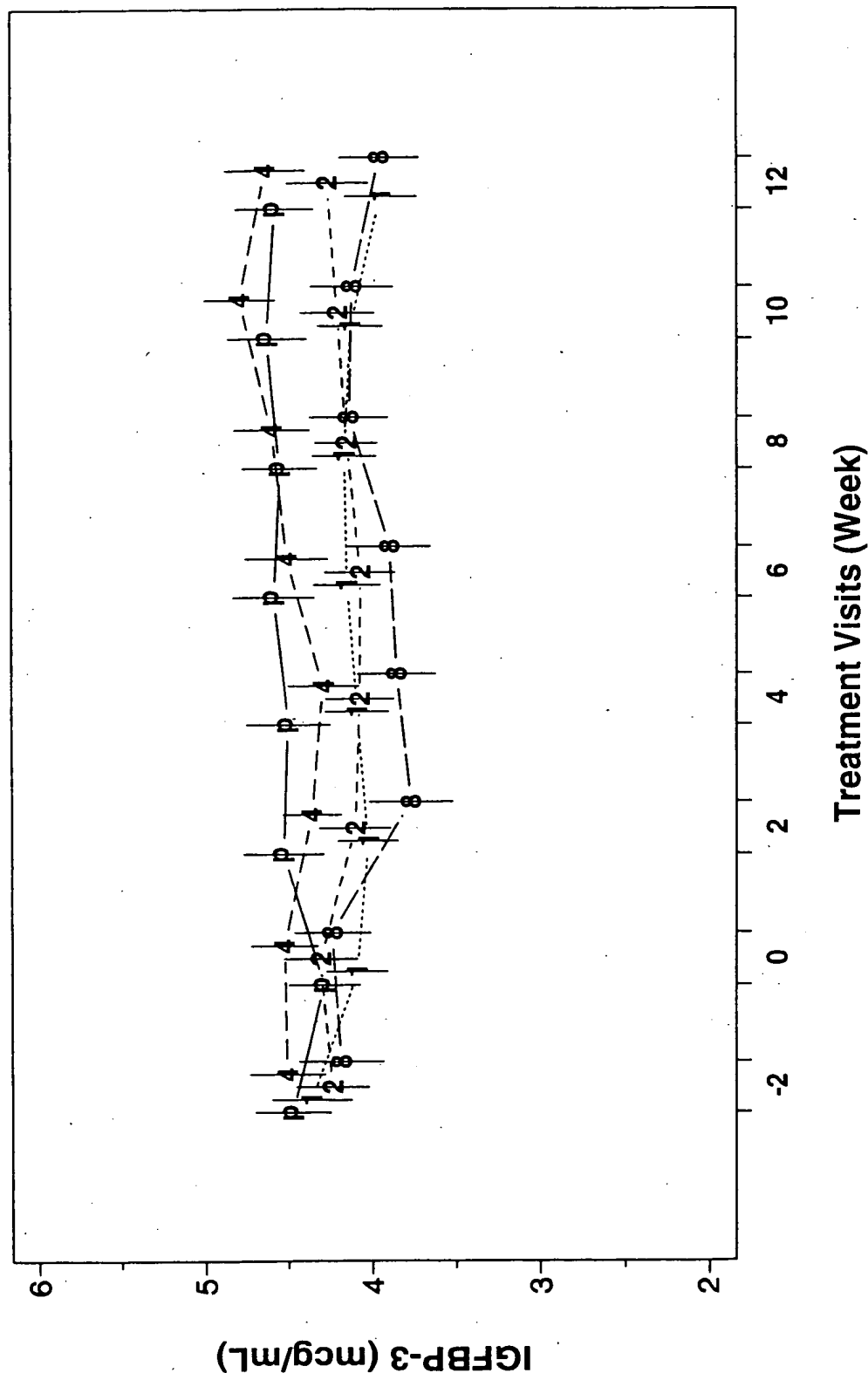


FIG. 44